UNIVERSITY OF TORONTO
MEDICAL JOURNAL

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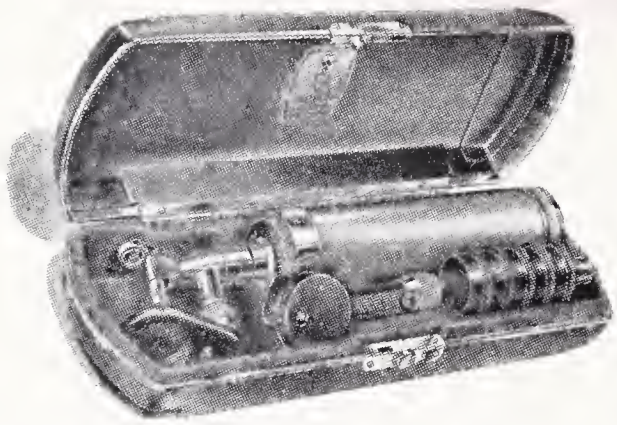

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1. Davis, C. H.: J.A.M.A. 157:126 (Jan. 8) 1955.

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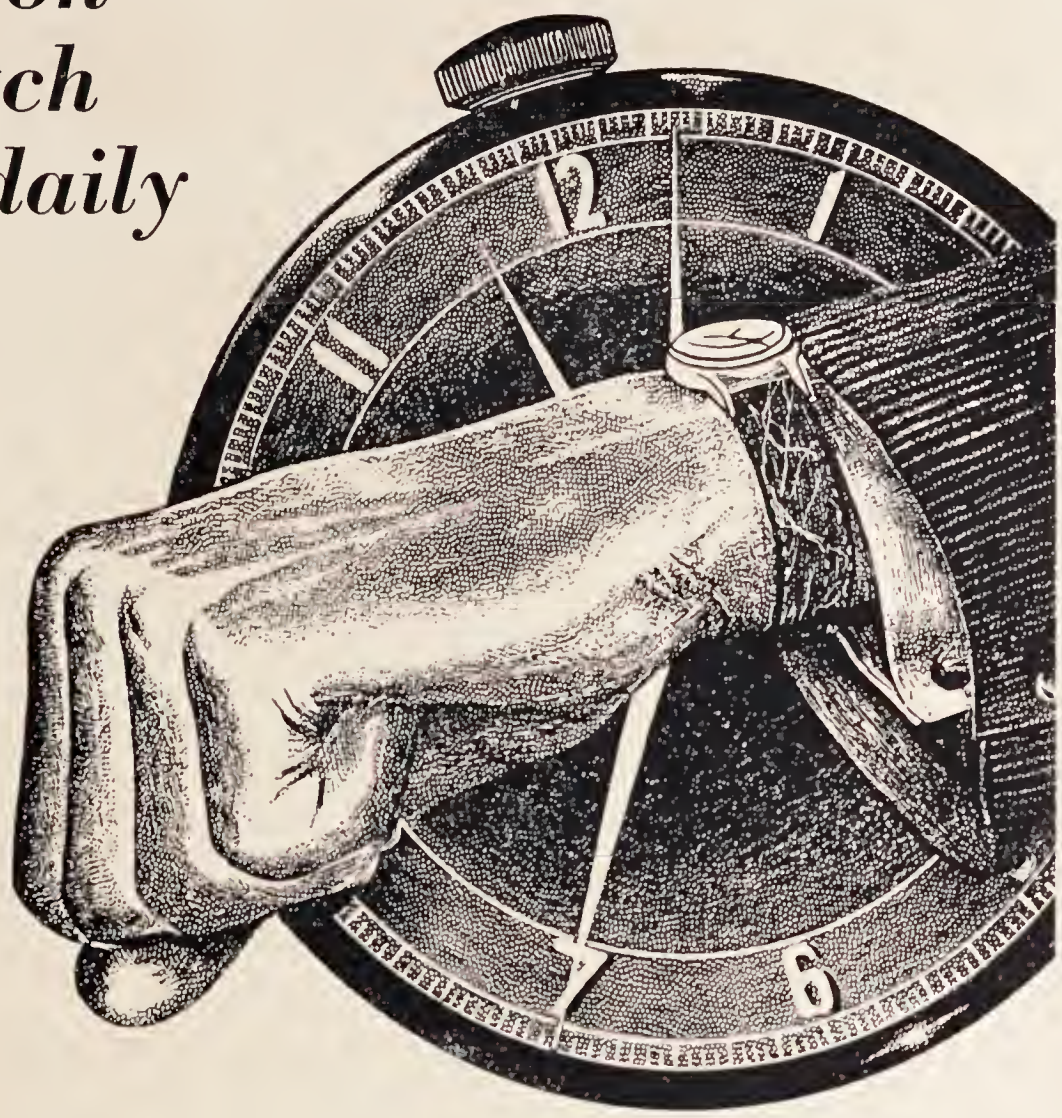

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Illustrations are included by arrangement with the Editor. Drawings should be done on white paper in black ink.

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EDITORIALS

The Crisis in Medical Journalism

Without its literature, medicine would stagnate as an art and perish as a science. The profession has recognized this for many years, and has vigorously encouraged the growth of medical journalism. And growth has occurred. So great, in fact, has been the expansion of medical literature, that now the volume of medical writing is reaching such unwieldy proportions that it is close to defeating its own purpose, viz: to inform. The present-day research worker is faced with literally hundreds of journals, each composed of numerous volumes; the specialist must read a dozen or more periodicals to keep informed just of his own specialty; and even the general practitioner, probably most in need of concise, easily obtained information, is confronted with a bewildering array of review publications. Clearly, a crisis is developing in medical literature.

To add to the confusion, many journals are losing sight of their aims, and are publishing articles which properly belong in other publications. A journal devoted to physiological problems may publish a paper dealing with a clinical question related only remotely, if at all, to physiology; a journal of a review nature may suddenly print results of original research. Such tactics, besides confusing the reader, lead to the more dangerous situation in which a worker in a particular field may miss an important article unless he examines all publications instead of just those related to his own field.

At a recent conference of medical journalists, current medical literature was criticized on still another ground. It was generally admitted that the quality of contemporary medical writing is in many respects poor. This criticism was particularly directed to authors of papers and articles—writers who individually devote only a small part of their time to writing, but who collectively make by far the largest contribution to medical literature.

The present unfavourable trends in medical journalism must be reversed, or we are doomed to ever increasing confusion, overwork, and eye-strain. It should be axiomatic that no new journal should be started without a thorough evaluation of the need for the journal. Medical societies, research institutions, and clinics should not publish periodicals simply for the sake of having their own publications. They should publish only if there is no outlet for their information already in circulation. Furthermore, every journal should have a specific aim in mind, and should adhere rigidly to that aim. It should exert careful judgment in its selection of material, and should reject material unrelated to its field of interest.

Finally, the problem of deteriorating quality in medical writing surely can be faced squarely and effectively. Good medical writing comes from education and practice. Few students will admit that they want more "English" taught to them, and this writer is loath to suggest it, but at least we can obtain practice in medical writing. It is the purpose, indeed the sole purpose, of the undergraduate journal,

to provide an opportunity for the student to learn about medical journalism. If we use this opportunity, we obtain at least an acquaintance with the principles of medical writing, and so contribute to the improvement of medical journalism. If we forsake this opportunity, we ignore the very real problems of the present-day literature of our profession.

J. Q. B.

Acknowledgment

The Editor wishes to thank Dr. W. F. Greenwood, Assistant Professor of Medicine, for his advice and assistance in the preparation of this issue.

The Webster Scholarship

The Academy of Medicine of Toronto is again offering the Webster Scholarship, of the value of fifty dollars, for the best undergraduate article appearing in the current volume of the Journal.

The Journal wishes to congratulate Dr. Ian Van Praagh, 5T5, who is the winner of last year's Webster Scholarship for his article entitled "Vertigo".

Volume xxxiii

In Volume XXXIII the Journal will follow the policy initiated last year of devoting each issue to a specific topic. The second issue of this volume is planned to deal with Infectious Diseases. Future topics will include Emergencies in Practice and Problems in Diagnosis.

We wish to remind our readers in the pre-clinical years that although some Journal articles may be of little interest to them at the present time, they may find it worthwhile to save their copies for future reference.

Students in the pre-clinical years who are interested in contributing articles to the Journal are urged to contact the Editor. Contributions from the pre-clinical years made by arrangement with the Editor are welcome, and their value is attested to by last year's excellent article on penicillin by Mr. A. C. Strickler, 5T8.

RHEUMATIC FEVER

A. D. McKELVEY, M.D., F.R.C.P.(C.)

RHEUMATIC fever is a disease which involves the connective tissues of the body, and which appears to be the result of an unusual state of sensitivity to the hemolytic streptococcus or some of its products. It is extremely variable in its manifestations, duration, severity, and ultimate effects. As the name implies, the most frequent manifestations are polyarthritis and fever. It may, however, present with any one or any combination of its major manifestations: arthritis, carditis, chorea, subcutaneous nodules, and erythema marginatum. Usually an attack, even when untreated, begins to subside after several weeks; but some cases continue to show signs of rheumatic activity for months or even years. The severity may range from cases in which it is difficult to decide whether the patient is sick at all, to acute fulminating fatal illnesses. However, it is the subsequent development of rheumatic heart disease, often years after the acute attack, which is responsible for most of the serious disability resulting from rheumatic fever. Curiously, there is no consistent correlation between the severity of the acute attack and the likelihood of later cardiac disease, although there does appear to be a definite correlation between the number of recurrent attacks and the incidence of rheumatic heart disease.

Etiology

The cause of rheumatic fever is still not clearly understood, although its relationship to infections with Group A *beta* hemolytic streptococci has been definitely established. The acute attack is nearly always preceded by a streptococcal infection, but there is very little correlation between the severity of the streptococcal infection and the probability of developing rheumatic fever. Once an attack of rheumatic fever has commenced, eradication of the streptococci does not halt the attack. There is usually a latent period of from one to three weeks between the streptococcal infection and the onset of rheumatic fever. Nearly all of us have had infections due to hemolytic streptococci, yet only a small proportion of the population ever develop acute rheumatic fever. Because of these facts and other laboratory evidence we believe that the disease is an abnormal tissue reaction in a person with an unusual sensitivity to hemolytic streptococci.

This sensitivity may be a form of allergy. Why certain people behave in this peculiar way is not known, but we do know that a patient who has recently had an attack of acute rheumatic fever is very likely to react in the same way and have a recurrence if he gets another streptococcal infection. With each year that passes without a recurrence, the likelihood of further attacks becomes less, and as the patient gets older the likelihood of recurrence also becomes less, as rheumatic fever is predominantly a disease of children and young adults. There are exceptions to this, however, and we had a man, forty-two years of age, who had a very serious attack of acute rheumatic fever.

The incidence of rheumatic fever varies with climatic conditions, and social and economic status. Generally, the incidence appears to parallel the incidence of streptococcal infections, and is higher in the colder damper temperate zones than in warmer drier climates. Similarly, there is usually an increased incidence in the colder damper seasons of the year. Living in over-crowded dwellings, and

possibly other factors such as malnutrition and increased exposure to cold, may be the explanation of the considerably increased incidenee among people in poor eeonomic circumstances. There were a large number of young serviee men who developed rheumatic fever while living in the close quarters of barrack life.

Clinical Features

In a disease with sueh variable features it is understandable that there may be considerable doubt in some cases whether a given patient has rheumatie fever. In an attempt to clarify this problem, the late Dr. T. Duckett Jones published criteria for the diagnosis of rheumatic fever in 1944 which have been widely accepted (1). He classified the clinieal manifestations into major and minor categories, depending on their relative oecurrence in rheumatic fever and other diseases from which this disease must be differentiated. The division into major and minor categories has no significance beyond the relative importance of each manifestation in making the diagnosis, and has nothing to do with the severity of the disease or its outlook.

Using these criteria Dr. Jones stated that the presence of two major manifestations or of one major and two minor manifestations indicated a high probability of the presence of rheumatie fever. The clinical manifestations of the disease are discussed under the headings Dr. Jones proposed, with slight modifications reeently suggested by the American Heart Association (2). We must beware, however, of attempting to apply such a scheme too rigidly, as it is intended to serve only as a guide to what is often a very difficult elinical problem.

MAJOR MANIFESTATIONS

1. *Polyarthritis* Characteristically this is a flitting arthritis. One joint may be clearing up at the same time as another is beeoming involved. The joints may be extremely inflamed, swollen and tender; or they may be only painful without any objective signs of involvement. There is frequently an effusion into the involved joint which is always sterile on culture. When the joint symptoms subside there is very rarely any permanent joint damage.

2. *Carditis* Pathologically, rheumatic fever can involve all three layers of the heart, pericardium, myocardium, and endocardium, so that we can describe it as a pancarditis.

Rheumatic pericarditis is one of the common forms of acute pericarditis, but if other evidence of rheumatic activity is not present it may be difficult to differentiate from the other two common aeute types, idiopathic pericarditis and tuberculous periearditis. A pericardial friction rub may be heard. The electrocardiogram may show changes usually in the ST segments and T waves. If a pericardial effusion develops it is a sterile exudate, and occasionally may cause cardiae compression requiring paracentesis.

Cardiac enlargement oceurring during an attaek of rheumatie fever may be due to myocardial involvement, pericardial effusion, or the eardiae dilatation seen with valvular lesions or congestive failure. Serial x-rays may show a marked increase in cardiac size, which sometimes returns to normal when the attack has subsided, and which in other cases remains permanently increased.

Congestive heart failure may develop in a patient with active rheumatic fever even when there is no evidence of valvular disease. The most common manifestations are an elevation of the jugular venous pressure and an enlarged liver. It is frequently accompanied by a taehycardia.

Cardiac murmurs are particularly sig-

nificant if it is possible to determine that they are of recent development, or that they are changing. They may be due to valvular abnormalities such as aortic incompetence which causes an aortic diastolic murmur, or mitral incompetence which causes a mitral systolic murmur. The latter may be due either to dilatation of the mitral valve ring, or inflammation of the valve. If this murmur is loud and long, almost half the patients will subsequently develop rheumatic heart disease. Faint soft or blowing systolic murmurs are heard at the apex in many normal people, and with even greater frequency in patients whose cardiac output is increased as it is with any febrile disease, so that their significance is much harder to interpret, and they do not have such a serious prognostic import.

A soft mitral diastolic murmur developing during an attack of acute rheumatic fever is usually evidence of carditis. Under these circumstances it is probably due to enlargement of the left ventricle, or possibly to some involvement of the mitral valve. Mitral stenosis usually takes at least several years to develop after the initial attack of rheumatic fever. It, of course, can also produce a mitral diastolic murmur, but it is usually a lower pitched rumbling murmur with a presystolic accentuation.

3. *Chorea* This manifestation of rheumatic activity often occurs alone without any other major or minor manifestation. The patient has uncontrollable, jerky, incoordinated movements, which may range from occasional slight twitches to continuous gross thrashing movements of such severity that the patient may injure himself or throw himself out of bed. There may be alterations of the tendon reflexes so that extension is sustained for an appreciable time. There is often difficulty in writing and holding small objects, and the patient appears to be clumsy. Sometimes there is an emotional disturbance accompanying it.

4. *Subcutaneous nodules* These are small subcutaneous nodules which are usually attached to fascial structures such as tendon sheaths or joint capsules. Common locations are the elbows, knees, back of the head and the knuckles.

5. *Erythema marginatum* This is a form of *erythema multiforme*, and consists of circular, oval, or irregular rings with a thin red margin usually surrounding apparently normal skin. It occurs mainly on the trunk and the proximal parts of the limbs. The lesions tend to come and go, often for a considerable period of time.

MINOR MANIFESTATIONS

1. *Fever* In the majority of cases the temperature is elevated at some stage of the disease. The duration and height of the fever are extremely variable, and some cases never have a significant elevation of temperature. Persistent fever usually indicates that the inflammatory process is still active.

2. *Sedimentation rate* This is another index of the activity of the inflammatory process. It usually is slower to rise than the temperature and persists longer. Regular weekly determination of the sedimentation rate, if carefully performed, is one of the most valuable guides to the course of the disease.

3. *PR Interval* There may be a delay in the conduction of the impulse from the auricle to the ventricle causing a lengthened PR interval in the electrocardiogram. Normally the upper limit is considered to be 0.20 sec. Cases with carditis often have a prolongation of the QT interval as well.

4. *Arthralgia* When no objective findings in the joints can be observed, but

the patient has pain which is clearly located in the joint, we can use this feature as a minor criterion in diagnosis.

5. *Evidence of a preceding beta hemolytic streptococcal infection* This may be based on a typical clinical picture, or it must be confirmed by culture of the organism or demonstration of an elevated or rising antistreptolysin—0 titre.

6. *Previous history of rheumatic fever or the presence of inactive rheumatic heart disease.*

Prognosis

Bland and Duckett Jones have reported an excellent twenty year study of one thousand cases followed since childhood (3). These patients, all under the age of twenty, were first seen during the period 1921–31 with rheumatic fever, chorea, or rheumatic heart disease. On recovery from the initial illness, 653 patients (65%) had signs of rheumatic heart disease. Twenty years later 108 of these (16%) had no evidence of heart disease. Of the 347 patients (35%) who recovered from the initial illness without detectable heart disease, 154 (44%) had signs of valvular disease twenty years later. During the first ten years 202 patients died, and after the second ten years 301 had died. After twenty years 699 of the original one thousand patients were alive. The majority of these were well, and three-quarters of them had little or no limitation of activity.

Although our present methods of treatment might improve these mortality figures somewhat, (e.g. 10% of the deaths were due to subacute bacterial endocarditis, which was almost invariably fatal during most of the period covered by the study) these statistics are probably a fair guide to what we may expect to happen in the future to the cases we are seeing now. We should always bear in mind when considering statistics such as these, that the characteristies of any disease may be variable in different localities and at different times.

Treatment

There are two main points of attaek on this disease: treatment during the acute phase, and treatment aimed at preventing attacks. It is probably in the latter that the most important therapeutic advances have been made in recent years.

Treatment during acute phase

For over fifty years it has been known that salicylates can produce a marked improvement in certain of the manifestations of acute rheumatic fever. This effect is mainly on the exudative features of the disease; the fever, and the pain and swelling in the joints usually subside quickly. However, the proliferative lesions, and these include carditis, are much more resistant to salicylates. It is not known definitely whether salicylates have any effect in preventing the lesions which later lead to chronic rheumatic heart disease. Nevertheless, the improvement is often very prompt and dramatic, and the patient is made much more eomfortable.

When cortisone and ACTH became available, it was soon found that they also produced a dramatic improvement in many cases. It was hoped that they might prove to be more effective than salicylates in treating carditis and preventing the subsequent development of rheumatic heart disease. Because some of the most important of these lesions, e.g. mitral stenosis, take years to develop, this question has been very difficult to answer, and it is not yet definitely settled. An extensive cooperative study has been carried on for over four years in thirteen centres in the United States, the United Kingdom, and Canada, in an attempt to get data on the relative effectiveness

of salicylates, cortisone and aspirin (4). Toronto was one of the study centres chosen, and patients from the Hospital for Sick Children and Toronto General Hospital were included in the series. Altogether approximately five hundred cases in children were studied, and the results of treatment during the acute phase and first year following treatment have been reported. There was no evidence that any of the three agents (aspirin, cortisone or ACTH) resulted in uniform termination of the disease, and on all treatments some patients developed fresh manifestations during therapy. Treatment with either of the hormones resulted in more prompt control of certain acute manifestations, but this more rapid disappearance was balanced by a greater tendency for the acute manifestations to reappear for a limited period upon cessation of treatment. At the end of one year there was no significant difference among the three treatment groups in the status of the heart. During the period of treatment, observation, and one year of follow-up there were only six deaths among 497 cases under the age of 16 admitted to the study.

Investigation is continuing here and in other centres; and different treatment schedules with varying dosage, duration of treatment, and combinations of drugs are being tested. It is evident, however, that adequate treatment for this disease is not yet available.

Salicylates have the advantage of being the simplest to administer, having less serious toxic effects, and the patients are less likely to have a flare-up when treatment is stopped. The dosage is usually between one-half and one grain per pound of body weight per day. Adults and larger children generally tolerate less of the drug in proportion to weight than do small children. Alkali may be given to reduce the gastric irritation and the acidosis that may occur with large doses of salicylates, but the tendency now is to omit alkali, as there is evidence that it reduces the absorption of the drug.

Patients are usually kept in bed, and given aspirin or hormone therapy until all signs of activity have subsided. The sedimentation rate is often the last sign to return to normal. Then a gradual program of convalescence and return to normal activities is started.

Unless they have developed serious heart damage, these patients are usually able to lead a normal life after their disease has subsided.

In addition to the general measures mentioned, individual manifestations such as congestive failure must receive the appropriate treatment. Chorea may require heavy sedation. An adequate diet, comfortable surroundings, and plenty of encouragement are particularly important, since the illness is usually a prolonged one.

PROPHYLACTIC THERAPY

The role of hemolytic streptococcal infections in causing rheumatic fever has a very important practical application in the prevention of the disease. Since there are as yet no methods of treatment available for the acute attack of rheumatic fever that can be relied upon to prevent heart damage, the importance of preventing the disease is obvious. Fortunately beta hemolytic streptococci are practically always sensitive to penicillin and usually sensitive to sulfonamides. There are two main lines of attack on the problem:

1. The prevention of recurrence in the patient who has had an attack of rheumatic fever.

2. The prevention of the first attack.

In the first group it has been shown that small doses of sulfonamide (e.g. Sulfadiazine 0.5 gms. daily for a child

under 60 lbs. and 0.5 gms. twiee daily for an older ehild or adult) administered eontinuously throughout the year redueed the recurrenee rate to about one-tenth the rate in eontrol series of patients not given prophylactie therapy. A large number of carefully eontrolled series have eonfirmed these results, and it now should be standard praetiee to administer some form of prophylaetie therapy against hemolytie streptoeoecal infection to every patient following an attaek of aeute rheumatie fever (5, 6). This therapy should be maintained eontinuously until the age of eighteen years, or for at least five years after the last attaek. Sulfadiazine is probably the eheapest and easiest drug to administer, but a few patients will develop toxie reaetions. Periodie eheeks of the urine and white blood eount are essential, espeeially during the first few weeks of therapy. Penieillin (either oral dosage of 200,000 units twiee daily or by intramuseular injeetion of one of the very long acting preparations sueh as Bieillin L.A. 1,200,000 units every two to four weeks) has also given very good results, and may possibly be even more effective than sulfonamides with less risk of toxie reaetion (7).

The prompt reeognition of infeetion due to hemolytie streptocoeei and the early institution of ehemotherapy may also be effeetive in redueing the ineidenee of rheumatie fever (8, 9). However, this is more diffieult to prove as probably there has been a gradual dereease in the ineidenee of aeute rheumatie fever going on for about twenty years, and the incidenee aetually started to decline before sulfonamides were widely used.

Conclusions

Rheumatie fever still presents many problems to the elinieian. It may at times be an extremely diffieult condition to diagnose. In such eases, applying Dr. Jones' eriteria may give one a useful starting point from which to evaluate the signs and symptoms. In the field of therapy the relative merits of aspirin and the hormones is still eontroversial. Certainly none of our present methods of therapy is really adequate. Probably the greatest advanee in reeent years has been in the prevention of reeurrent attaeks by prophylactie sulfonamide or antibiotie therapy.

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SUBACUTE BACTERIAL ENDOCARDITIS

D. C. STEELE, 5T6

SUBACUTE bacterial endocarditis, as a clinical entity, is far commoner than the more malignant acute form of endocarditis. Until the advent of modern antibiotics and chemotherapy, a diagnosis of this disease carried an almost hopeless prognosis. Less than three per cent of recognized cases recovered spontaneously. Today, however, the outlook is no longer hopeless, and early recognition of the disease coupled with vigorous therapy may be expected to effect complete and permanent remission in the majority of cases.

BACTERIOLOGY

The organism responsible for subacute bacterial endocarditis is the Streptococcus viridans in 90 to 95 per cent of cases, and in the remainder of cases is the Streptococcus faecalis, Gonococcus or influenza bacillus. Among the less common infecting organisms are Spirilla, Staphylococcus, E. coli, B. pyocyaneus, Monilia, Histoplasma and Micrococcus pharyngis siccus. Those organisms of the viridans group commonly associated with subacute bacterial endocarditis are the Streptococcus salivarius, isolated from about one-third of cases, the Streptococcus mitis, Streptococcus bovis and Streptococcus S.B.E. The last named has been isolated from cases of bacterial endocarditis only, and its normal habitat is unknown. A few so-called sterile cases of subacute bacterial endocarditis have been reported, but it would seem that in these instances the sterility is more apparent than real. It may be that the bacteria are more deeply implanted in the affected tissue than usual, and therefore do not have ready access to the blood stream. Why this should occur is as yet unclear.

PATHOGENESIS

Bacterial invasion of the blood stream is much commoner than one might suspect. Transient bacteremias are common during upper respiratory and urinary tract infections. The permeability of the gastrointestinal tract is well illustrated by the fact that Bacillus prodigiosus, when fed with a meal, can be recovered from the blood stream. Streptococcus viridans bacteremia is common after the manipulation of an infected tooth, tooth extraction or tonsillectomy. Other portals of entry include the prostate, cervix, puerperal uterus, hemorrhoids, wounds, necrotic cancers, tuberculous cavities, bed sores and skin infections.

The entry of streptococci of low virulence into the blood stream is relatively innocuous unless the bacteria lodge and proliferate on the endocardium. As a rule, this occurs on valves scarred by rheumatic fever or on those congenitally malformed. Occasionally, the streptococci lodge in an arterio-venous aneurysm, a patent ductus arteriosus, or at the site of a coarctation of the aorta. The infection in these instances is known as subacute bacterial *endarteritis.*

In subacute bacterial endocarditis, the valve most commonly affected is the mitral, followed in frequency by the aortic. The tricuspid and pulmonary valves are involved in only 15 per cent of cases. The lesions consist of flat cauliflower-like excresences containing fibrin, platelets, and other inflammatory products in which the streptococci are imbedded. They are situated near the free edge of the valve at the line of closure, on the cordae tendineae, and occasionally on mural endocardium. The method

of implantation of the infecting organism is open to question. The fact that the process usually occurs in a previously damaged heart suggests that a roughened endocardium or some degree of vascular insufficiency in a valve may be factors in the establishment of a lesion. If such is the case, inoculation probably occurs from the main blood stream within the heart chambers. Implantation may occur through the vessels supplying the valve in some instances.

In any event, when the bacteria are deposited on or within a valve, they proliferate, and this proliferation stimulates the deposition of platelets and fibrin upon the valve, with the formation of a vegetation. The valve leaflet undergoes gradual necrosis, and granulation tissue grows into the vegetation. The new capillaries accompanying the granulation tissue seldom reach the periphery of the lesion, and for this reason the clumps of bacteria within it are relatively safe from the phagocytic action of leucocytes. This may partially explain the difficulty experienced in treating the infection.

From these vegetations, organisms are continuously shed into the blood, but owing to their low virulence are easily removed by the cells of the reticuloendothelial system. The vegetations themselves are very friable and may break off and be carried along as arterial emboli.

CLINICAL FEATURES

The subacute form of bacterial endocarditis occurs in 10 to 25 per cent of patients with chronic rheumatic heart disease and in approximately 25 per cent of those with interventricular septal defects. A history of low grade fever, chills, malaise and weight loss in a patient who has rheumatic or congenital heart disease should immediately arouse suspicion of subacute bacterial endocarditis. Indeed, it should be considered in every patient with persistent fever and a heart murmur. If diagnostic error is to be made, it should be one of overcaution rather than neglect.

Endocardial inflammation is to be regarded not only as a localized reaction to a parasitic organism and its toxic products, but also as a systemic reaction, and for this reason the clinical picture of subacute bacterial endocarditis is only evidence of sepsis producing its major changes in an organ particularly able to give clinical evidence of its pathology.

In approximately one-third of cases symptoms develop one to three weeks after some other illness such as an upper respiratory infection, or often after some operative procedure such as tooth extraction or tonsillectomy. No truly typical clinical picture can be described, varying as it does with the chance distribution of emboli and pre-existing cardiac disease. The onset of symptoms may be slow and insidious or very stormy, the latter occurring in about 25 per cent of cases. The patient may complain of weakness, fatigue, malaise, weight loss, sweats, pain in the joints, parasthesias or paralyses. Fever may be high, low, or even absent for long periods. Precordial pain of a sticking nature, or a feeling of oppression may be the only symptoms referable to the heart. However, a tachycardia out of proportion to the patient's temperature is a significant finding.

On physical examination the patient will usually appear chronically ill. Pallor is characteristically present. The dull white sallowness has been aptly described as *café-au-lait*, and is due to a hypochromic microcytic anemia. Small petechial hemorrhages can occur anywhere in the body, but are especially frequent on the mucous membranes of the palate, buccal mucosa and conjunctiva. Splinter hemorrhages may occur near the distal margins of the nail beds. Their name derives from their linear

shape and their resemblance to imbedded splinters. In the pulps of the fingers, small, painful, reddish areas may develop and vanish in the course of one or two days. These are known as Osler's nodes. The appearance of larger, painful, erythematous areas on the soles of the feet or the palms of the hands is not unusual. If the disease has been present for some time, clubbing of the fingers may have occurred. The spleen is palpable in 50 per cent of cases, and is occasionally tender if there has been recent splenic infarction. The cause of the joint pain present in 25 per cent of cases is as yet undecided. Changing heart murmurs have often been mentioned as being of diagnostic significance, but their presence is too variable to be of much value.

The signs of embolism are, by the nature of their origin, sudden and striking. These emboli do not characteristically lead to liquefactive necrosis. Those lodging in the cerebral arteries may lead to hemiplegia, and in any hemiplegia in a young person this cause must be considered. Emboli to the spleen, with a resultant perisplenitis, are common. The "flea-bitten" kidney, seen almost routinely at autopsy in cases of subacute bacterial endocarditis, is the result of many small emboli which have lodged in that organ, producing an embolic nephritis with hematuria and albuminuria. Emboli may lodge in the retinal artery, causing blindness in one eye. They may rarely occur in the coronary arteries, and are not uncommon in the arteries of the extremities. Osler's nodes are the result of microscopic emboli.

LABORATORY FINDINGS

Laboratory investigation is a strong aid to diagnosis. The most specific diagnostic measure is the blood culture. Two to four samples should be taken daily during the first two or three days. If chills, spikes of fever or new crops of petechiae occur, blood cultures should be obtained during these episodes. It is doubtful if cultures of arterial blood are superior. Those of the bone marrow are undoubtedly so and, along with urine cultures, probably should be obtained routinely if blood cultures prove sterile. Often the organism is recovered from the urine, and in some instances sooner than from the blood. If the patient has received prophylactic penicillin the laboratory must be notified. The leucocyte count is often elevated above 10,000, although a leucopenia is not uncommon. The erythrocyte sedimentation rate is usually elevated. The electrocardiogram is not pathognomonic, and abnormal tracings are the result of preceding cardiac disease.

TREATMENT

As previously mentioned, subacute bacterial endocarditis, before the advent of antibiotics, was almost invariably fatal. Death occurred from embolism, uremia, cardiac failure or the exhaustion of the reticulo-endothelial system. Vigorous treatment will now lead to recovery in many cases. Still, the ultimate prognosis is poor, because those surviving the overwhelming infection are left with their previous cardiac disease plus further damage from the superimposed endocarditis. Residual changes may have occurred in the kidney and other organs as well. For these reasons 20 to 30 per cent of treated cases will succumb or suffer a varying degree of ill health.

Inasmuch as the large majority of infective organisms responsible for subacute bacterial endocarditis are susceptible to penicillin, an eradication of the disease may be expected in 80 to 90 per cent of cases treated with this antibiotic. In some cases of penicillin-resistant organisms, other antibiotics, or a combination of penicillin plus strepto-

mycin, are effective. The major therapeutic concern is the initiation of a regimen of treatment which will be effective before irreparable damage has developed. At the present moment there is no method available whereby the response of any particular patient to therapy may be predicted. For this reason a dosage schedule ealculated to attain high blood levels of antibiotie must be initiated in all eases. It is true that in some cases this will result in over-treatment, but in a disease process as formidable as subacute baeterial endocarditis this fact is of minor importance.

Before the initiation of therapy, it is important, if at all possible, to obtain a positive blood culture. Without a positive blood culture it is difficult to cstablish an adequate dosage schedule, and premature treatmcnt may lead to confusion of the clinieal picture. Good clinical judgment is needed in deciding when therapy is to be instituted. An undue delay in trcating the case may lead to irreversible damage to the heart and other organs. In general, it may be stated that if the patient is desperately ill, and the physician is reasonably certain that the patient has the disease, there is no justification for delaying therapy until positive blood cultures and the results of sensitivity tests are obtained. Penicillin is the antibiotie of ehoice in these cases. Even after therapy has commeneed, blood cultures must be taken at frequent intervals and kept for at least three weeks.

When the *in vitro* sensitivity of the infecting organism is determined, one must strive for a blood level of antibiotic which is five times this scnsitivity. For practical purposes a dosage of one million units of penicillin may be considered to give a blood level of one unit. Aqueous penicillin G (or the potassium salt, in patients with cardiac failure) is highly effective.

The method of administration is a matter open to discussion, and is probably best dictated by individual circumstances. Two courses may be followed —the maintenance of a continuous high blood level of penicillin, or the production of intermittent vcry high levels. The latter method is based upon the assumption that since penicillin, to be effective, must act over several cell divisions, intermittent levels will allow a division of the bacteria bctween doses, thus rendering the antibiotic more effective. This is possibly the more effective method. However, thc disease may be treated successfully by the production of a constant blood level with proeaine penicillin. A basic sehedule which may be followed is the administration intramuscularly of 600,000 units of crystalline penieillin G plus 1,800,000 units of procaine penicillin daily in four divided doses. Although the intramuscular route of administration has certain recognized disadvantages, it is to be preferred to the intravenous administration whose chief drawback is venous thrombosis. By varying the site of injection the discomfort to the patient will be reduced.

After therapy has commenced the clinical response is observed carefully from day to day. If the regimen is effective blood cultures usually become sterile in four or five days. If they do not, a change of dosage or of drug should be considered. Penicillin plus streptomycin, or a wide spectrum antibiotic sueh as Aureomycin, may be tried. Within two to three days defervescence usually occurs, the pulse rate falls, and the patient feels well. Although the hemoglobin level gradually rises and the sedimentation rate gradually falls, they may not return to normal limits for several weeks. Emboli may also occur for several weeks at the beginning of convalescence. Heart murmurs often change, and may vanish completely.

Ordinarily, treatment should be continued for a minimum of six weeks, or eight weeks if the outlook seems poor. In some cases where ten to twelve million units of penicillin combined with two grams of streptomycin have been given daily, the duration of treatment has been reduced to two or three weeks. This procedure is experimental, however, and is not recommended as a general plan of treatment. In cases of subacute bacterial endocarditis due to Streptococcus faecalis, penicillin plus streptomycin is effective and should be given in doses of not less than 20 million units of aqueous penicillin G plus two grams of streptomycin daily for at least eight weeks.

The use of anticoagulants is mentioned only to be condemned, as it carries with it the hazard of bleeding at the site of embolism. If a very high level of penicillin is desired Probenecid (Benamid) is very useful, 0.5 grams being given every six or twelve hours. The effect of this drug is to delay the excretion of penicillin. It does not delay the excretion of streptomycin.

Complete bed rest is essential both before and after specific therapy. If cardiac failure is present, salt restriction is indicated. All possible reservoirs of reinfection should be eliminated during treatment.

Following recovery any major or minor surgical procedures (tooth extraction, childbirth, etc.) which might give rise to a transient bacteremia should be preceded by one million units of penicillin. This dose must be maintained for three or four days after the procedure. It might also be advisable to give two grams of Aureomycin each day in addition to penicillin to protect the patient against penicillin-resistant organisms such as Streptococcus faecalis. Surgical measures such as ligation of a patent ductus arteriosus should be considered in cases where this is the source of infection.

SUMMARY

Subacute bacterial endocarditis is reviewed under the headings of etiology, pathology, general features and signs and symptoms. The course and prognosis of the disease are discussed. Recent trends in therapy are outlined.

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GIANT-CELL ARTERITIS (Temporal Arteritis)

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THE term *temporal arteritis* is in general use to describe a clinical syndrome in middle-aged and elderly patients who suffer from an illness which has both generalized and focal manifestations. The pathological process distinguishes it from all other diseases of the blood vessels. This process has a predilection for the branches of the external carotid artery and, in particular, for the temporal branches thereof, and, accordingly, is generally referred to as temporal arteritis. However, it is almost always apparent that symptoms and signs are referable to other parts of the body as well. Furthermore, many patients at autopsy have now been found to have other arteries involved. Therefore, the term *giant-cell arteritis* is preferable.

The disease was delineated as an entity in 1932 by Horton, Magath and Brown. It is to be noted, however, that as long ago as 1890 Hutchison gave a perfectly adequate description of this disease in a report describing the eighty year old father of the beedle of The London Hospital. Owing to the fact that it is a disease of the later decades, it is undoubtedly increasing in its overall incidence. Further, the increasing frequency with which it is recognized is owing in part to the more widespread knowledge of its clinical picture. This is not an unusual or surprising phenomenon in medicine, nor indeed in any sphere of learning and understanding. As Goethe long ago remarked "*Was man weiss, sieht man*". The Surgical Pathology Department of The Toronto General Hospital had one biopsy-proved example of this disease up to the end of World War II, and ten have been added since that time. The sketch of this disease that follows is based largely on clinical experience with these ten patients.

Age of Onset

A diagnosis of giant-cell arteritis on clinical grounds in a patient under the age of forty-five will almost certainly be erroneous. From this age on its incidence increases, reaching a peak in the seventh and eighth decades.

Symptoms and Signs

1. systemic

Pain in the region of the temporal artery is common to many conditions. Migraine, "cluster" headaches, tension headaches and, indeed, most varieties of head pain can be maximal in this area. Furthermore, many of these conditions can be associated with a tenderness along the course of the temporal artery. Similar non-inflammatory processes can result in pain and tenderness in the area of distribution of the occipital arteries. One must not be misled by these superficial resemblances of all these conditions. The patient with giant-cell arteritis has a constitutional illness and subjective and objective evidence is almost invariably present. It is fairly safe to say that if the patient looks and feels well, he is almost certainly not suffering from giant-cell arteritis. General malaise and extreme fatigue have been common to all our patients. The majority have had joint pains which have varied from dull aching to severe pain with limitation of movement in various joints. The shoulders, hips and back are the common sites, although wrists, ankles and even feet have been affected. Epigastric distress, anorexia and weight loss have generally been found. Feverishness is not infre-

quently complained of, and most patients have had a moderate elevation of temperature.

These symptoms and signs of a generalized illness may precede by weeks, or even months, the local disturbances referable to the cranial arteries. In such cases it is exceedingly difficult to arrive at an accurate diagnosis.

2. HEAD PAIN

Headache of some type brings most of these patients to their physician. These headaches are extremely variable. They may be dull and generalized. When severe and excruciating they are usually localized to one side of the head in the temporal or occipital artery distribution. The patient may then complain of inability to wear his hat, his glasses, or to comb his hair, because of the tenderness of the skin. Sleep may be disturbed because this superficial tenderness in the occipital and temporal region prohibits a position of repose. Pain is usually steady with intervals of unbearably sharp exacerbations.

We have already made the observation that the blood vessels may be involved in a fairly general way. Nonetheless, the only vessels where striking superficial signs are to be found are the arteries of the scalp. The temporal arteries, and to a lesser extent, the occipital arteries, are very frequently, but not invariably, the site of tenderness, redness and some alteration in calibre. As a rule they are distended and may be pulsatile, or more probably pulseless. The redness and tenderness may be extremely segmental. Marked inflammatory change in the surrounding skin may be present and in some cases this may proceed to necrosis and even gangrene.

The head pain may be accompanied, or even preceded, by considerable face pain. This is usually a deep aching in the cheeks, or roof of the mouth, or jaws or teeth. Occasionally it is superficial and, therefore, vaguely suggests *tic douloureux*. Many patients consider that they have sinus or dental trouble.

3. OCULAR MANIFESTATIONS

The ophthalmic artery and its central retinal branch are frequently involved in the disease process. To account for this, one must recall that there is a good anastomotic connection between the internal maxillary branch of the external carotid artery and the ophthalmic branch of the internal carotid artery. Presumably the inflammatory process in the internal maxillary artery extends directly along the anastomotic pathway to the ophthalmic artery. This involvement leads to significant, and at times tragic disturbances of vision in about one-half of the patients. Visual loss is usually preceded by ocular pain. When this ocular pain is accompanied by fleeting visual disturbances, it is a most ominous sign, as vision may soon be lost or seriously impaired. Unilateral and bilateral total blindness may occur owing to occlusion of the ophthalmic or retinal arteries. The inflammatory, rather than the occlusive nature of the arterial process, may give rise to an optic neuritis and even a choroiditis from which some measury of recovery may be possible.

Laboratory Findings

A high sedimentation rate is almost an invariable finding. It is seldom found to be less than 100 mms. per hour by the Westergren method. This is usually accompanied by a slight rise in temperature, but not as a rule by any significant elevation of the white count. A normochromic normocytic anemia is very commonly found.

The pathological appearance is quite typical. An inflammatory reaction characteristically surrounds the vessel, as well

as infiltrating the adventitia and the media with lymphoeytes and plasma eells. All eoats reveal a varying amount of neerosis, and oeeasionally caleium is deposited in these areas. The internal elastie lamina beeomes fragmented, and a few to a great many giant eells ean be seen engaged in phagoeytosis of the fragments. The involved areas of the vessel are the site of extensive fibrosis. The lumina become narrowed and frequently thrombi form and obliterate the lumen when it beeomes suffieiently narrowed.

The Nature of the Disease

This is quite unknown. There have been those who regard it as a variant of periarteritis nodosa. The only justifieation for this is that in both conditions there is a generalized arteritis tending to involve arteries of the same size in association with a eonstitutional upset. The differenees are, however, more striking than these similarities.

If one examines the data from the eases who, pathologieally, are found to have a giant-eell arteritis, with a predileetion for the earotid braneh es, there are striking eharacteristies quite unlike those assoeiated with polyarteritis nodosa. The most important is the self-limiting nature of the disease, in marked eontrast to the vast majority of eases of periarteritis. Remission and apparent eure oeeasionally oeeur in typieal eases of periarteritis, but they are the rule in giant-eell arteritis. The average age of onset is also different; giant-eell disease oecurs only in the later deeades, while periarteritis oeeurs in any deeade, with most eases in early and middle adult life. Leukoeytosis is generally present and eosinophilia frequently so in periarteritis. Neither are striking findings in giant-cell arteritis.

Histologically, the diseases appear as distinet entities. Giant-eells and fibrosis eharaeterize the self-limiting disease, whilst neerosis and inflammatory cell infiltration are less eonspieuous. In periarteritis one occasionally sees a rare giant eell, and sees little fibrosis, whereas neerosis and inflammatory eells are very prominent. The affeeted vessels in periarteritis nodosa are notorious for aneurysm formation or rupture with serious and even fatal hemorrhage. To our knowledge, no rupture has oecurred from a site of giant-eell arteritis and only two aneurysms have been described.

Perhaps even more striking than all these differences is the response to treatment of giant-eell arteritis. Whereas one hopes with hormone therapy to arrest progress in the oeeasional patient with periarteritis nodosa, one can anticipate this with eonsiderable eonfidenee in the giant-cell disease.

Treatment

Three important facts must be borne in mind in eonsidering the therapy of this disease. First, it is a generalized, systemie arteritis, in whieh the ophthalmie and temporal vessels are only a part of the affeeted vaseulature. Seeondly, it is a disease that is known to run a self-limited eourse of several weeks to several months without tendeney to relapse and with fatalities oeeurring only where involved viseeral vessels thrombose. Finally, it is a disease of unknown etiology.

There would appear to be no doubt from our experience with these ten eases and from the few that have already appeared in the literature, that the most important weapon in therapy is eortisone. Seven of our own ten eases have been treated with this drug. One refused therapy; one was in the pre-eortisone days; one went into a lasting remission while we eonsidered the neeessity for this therapy. Within forty-eight hours of the onset of eortisone therapy the malaise

and fever subside and the pain begins to abate rapidly. In no case have we observed any advance in the disease while therapy has been continued. The contrast with the treatment of periarteritis nodosa is thus very striking.

The length of time that the drug will be required has to be worked out with each individual patient. In three of our cases the drug was stopped within two to ten weeks of its initial use and all had a prompt return of symptoms within forty-eight to seventy-two hours. In one of these, the exacerbation was alarming, as the patient developed severe pain in his one remaining useful eye. It would seem from these observations, and from the fact that the sedimentation rate remains elevated throughout therapy, that cortisone merely holds the disease in abeyance until it spontaneously remits. As a rule cortisone therapy is needed for a period of a few months, usually more than two and less than six.

Temporal artery sectioning, once proposed as a therapy for the relief of pain, is considered unnecessary save for diagnostic purposes, as cortisone will relieve pain. Furthermore, it is more satisfactory to have a systemic agent to attack a systemic disease. The severe and disabling constitutional symptoms of the disease will be entirely unaffected by local section of the artery.

THE MANAGEMENT OF CONGESTIVE FAILURE

D. E. WOOD, 5T6

CONGESTIVE failure may be defined as distress occurring when the heart is unable to perform its burden of work. Therapy is directed towards making the work minimal and obtaining maximum cardiac efficiency. As in the management of any condition, it is essential to make an accurate diagnosis before starting treatment. First, one must differentiate failure from other conditions which cause breathlessness or edema; then the type of heart disease leading to failure must be determined. This is important because some types of failure are amenable to specific treatment to such a degree that very little disability remains. Included are extra-cardiac causes such as anemia, thyrotoxicosis, myxoedema, and beriberi. Certain cardiac lesions, such as forms of congenital heart disease, constrictive pericarditis and mitral stenosis, are amenable to surgery. However, although it is rewarding to treat such cases, the opportunity is not frequently presented. More commonly, one's aim is to relieve the patient's symptoms so that he may return as nearly as possible to his normal life.

Two types of patients with congestive failure are seen. The first is the person who arrives at the emergency department in acute pulmonary edema. The second is one whose condition has arisen more gradually; he is chronically rather than acutely ill. The treatment of the first group of patients, once the emergency has passed, is the same as that of the second group. Therefore, the treatment of acute pulmonary edema and chronic congestive failure will be considered.

Acute Pulmonary Edema

Treatment of acute pulmonary edema is an emergency. Quickly, one must help the patient out of his acute dyspnea to prevent death. Regardless of how drastic the patient's condition may appear, treat-

ment should be begun, since with vigorous therapy a response ean be obtained even in moribund patients.

Morphine sulfate should be given immediately. It relieves dyspnea partly by sedating and partly by reducing the sensitivity of the respiratory eentre to the afferent impulses of the Hering-Breuer reflex. The dosage is one-quarter of a grain. One may use smaller doses in elderly or frail patients. Demerol may be used; but sinee it does not produee the same euphoria, a desirable attribute, morphine is preferred. Some elinicians suggest the routine use of atropine with morphine. It aids the drying of secretion and also reduees the possibility of nausea and vomiting. The suggested dose is one-one hundred and fiftieth of a grain. However, this is not a proven proeedure and should not be earried out routinely.

Oxygen should be started as soon as possible. Although any method is satisfaetory, the most certain route of administration is by nasal eatheter, with the flow regulated at approximately six to eight litres per minute. If fluid aceumulates, the oxygen may be bubbled through aleohol. This acts as an emulsifying agent, redueing the surface tension, so that foam will evaporate. It is easily administered by replaeing the water whieh is normally used for humidifiea-tion with absolute alcohol. If a mask is used, fifty per eent alcohol in water is preferred. Two precautions should be observed: when starting, the flow must be inereased gradually—sudden application irritates the mucous membranes; the use of aleohol should not be continued indefinitely—excessive absorption sedates the patient unduly. If large quantities of fluid are present, suetion should be used to elear the airway.

The eardiac glyeosides and the diureties are both of great importanee in the treatment of congestive failure. Sinee there is a delay in the aetion of these drugs, they should be administered immediately so that they will be effective as soon as possible. They will be eonsidered subsequently.

When the patient is first seen he will be in the position in which he is able to breathe as freely as possible: the orthopneic position. He should be encouraged to maintain this position, either in an easy chair or in bed, with his legs dependent. Venous tourniquets may be applied to the patient's legs and, if necessary, to the arms, to pool the blood. Isehemia will not be a problem if the tourniquets are released at definite intervals of fifteen minutes. If the above measures do not appear to be effective, venesect! Rapidly remove three to five hundred cc. of blood; the amount is estimated by the relief obtained by the patient. It has been said that a venesection without blood on the floor is too slow to be effeetive. It may be done either with a No. 16 needle in a vein and a suetion bottle, or with a blood pressure euff on the limb at diastolie pressure and ineision of the vein with a sealpel.

Aminophylline may also be useful. It relaxes the bronehial musculature, stimulates the myoeardium, and aids diuresis by increasing glomerular filtration. However, it has the disadvantage that it may eause vomiting. One-half Gm. in 10 ee. of 5% glucose is given intravenously, slowly.

Chronic Congestive Failure

The average patient in congestive failure requires less extreme measures. In faet, a minimum of proeedures are attempted so that the patient is disturbed as little as possible. Basieally, there are three aspeets to therapy: rest, digitalis, and eontrol of salt and water balanee through the use of diet and diureties.

Rest is very important in the treatment of the patient with eongestive

failure. Rest should be both mental and physical. The value of hospitalization must be determined for the individual patient. Early in congestive failure only moderate curtailment of activity at home is necessary, but with advanced failure, careful nursing is required and admission to hospital is indicated. In addition to the severity of the failure, psychological factors must be considered. One person may find relief from tension by hospitalization; another may be unduly disturbed by hospital surroundings and routine. Whether at home or in the hospital, the patient requires adequate sedation. During the day, if he is anxious and distraught, he should receive phenobarbital one-half grain three times a day. During the night, if dyspnea prevents sleep, the drug of choice is morphine. This does not mean that the usual sedatives, the barbiturates, chloral hydrate, paraldehyde, have no place; but rather that both types of drugs should be used discriminatively.

Whether it is desirable to enforce complete bed rest in moderate congestive failure is debatable. The advantages of complete rest must be weighed against the risks of thrombosis, stasis, and difficult ambulation. An excellent compromise is the daily use of the bedside commode. The increase in exertion, if any, is slight, and the relief of the emotional and nursing problems is considerable. The bowels should be kept regular. If the patient has become accustomed to a particular laxative he should be allowed to use it; if he fears constipation, or is straining at stool, a new laxative should be prescribed. If needed, an enema should be ordered every other day.

Any patient confined to bed should do foot and breathing exercises and should change his position frequently to prevent thrombus formation. These patients are especially liable to thrombosis because of the distress caused by moving and the stasis in peripheral circulation. Some authorities have advocated the use of anti-coagulants; however, if the failure is treated vigorously and the patient becomes ambulatory in a few days it is not necessary.

The physician should know about previous use of digitalis or its derivatives. When none has been taken in the past two or three weeks, it is reasonable to assume that no effect remains. With more recent administration, or when the previous dose is unknown, it is wise to proceed with caution. In either instance, digoxin is the drug of choice, because it acts quickly and the response can be observed rapidly. If over-dose is given, the drug is rapidly excreted and the toxicity soon passes. A dose of 0.25 mg. is used first. If no ill effects ensue, the drug may be pushed further until full benefit is obtained, or toxic signs develop.

Although in acute failure digoxin may again be used, it is claimed that Lantoside C acts in a shorter time, and, therefore, is more valuable when time is short. The first dose, 0.4 mg., is repeated at intervals of two hours, depending upon the response. A total of 1.0 to 2.0 mg. in four to eight hours is customary. The drug may then be changed to a longer acting preparation. Ouabain (Strophanthin) acts even more rapidly than Lantoside C, but is not commonly used on this continent. There is a greater risk in the intravenous use of Ouabain, and the slightly more rapid action is seldom necessary.

In the average case, where the patient is known to be undigitalized, and where he does not need rapid digitalization, there is no advantage to intravenous preparations. Although many programs are suggested, generalizations do not fit a specific patient; any schedule must be flexible. The relative advantages and dis-

advantages of the different preparations are debatable. While advocates of purified forms such as Digitoxin and Gitaligen claim that they produce fewer gastro-intestinal symptoms than the crude leaf, this may be a disadvantage. These comparatively unimportant symptoms provide warning of overdosage and help to prevent more drastic sequelae. Probably there is no disservice to the patient when either is prescribed and, since the leaf is cheaper, it may be the more desirable. Since doses vary so much from individual to individual, the saying "three grains three times a day for three days" is convenient. When the medication is prescribed after meals the patient is given the option of refusing it if he has not eaten well. Anorexia being an early symptom of toxicity, the probability of overdosage is reduced. Once the patient is digitalized (therapeutic effect without toxicity), a maintenance dose is prescribed. Normally it lies in the range of 0.1–0.2 Gm. daily, *per os*. If Digitoxin is preferred, the above doses will be accurate if they are divided by 1000.

The toxic manifestations may be divided into two groups: gastro-intestinal, and cardiac. The earliest to appear are usually anorexia, nausea, and occasionally diarrhea. Cardiac injury is more serious. The earliest sign is the occurrence of extra-systoles, which may lead to *pulsus bigeminus* and later paroxysmal auricular tachycardia. With this rapid rate it might be tempting to give more digitalis, making the situation worse. Again, overdosage may be signified by excessive ventricular bradycardia in auricular fibrillation. The ECG shows ST depression with inversion of the T waves and increase in the P-R interval; later, signs of complete heart block develop. Under these circumstances the glycosides should be discontinued. If the poisoning is severe, potassium salts (4–12 Gm. daily) may be helpful. One finds the classic symptom of yellow vision only rarely.

The immediate problem of nutritional management is to reduce the work load of the heart, and to eliminate or prevent abnormal water and sodium storage in the extracellular spaces. The diet must strike a balance between the desired minimum salt intake and the problems of practical dietetics. At first, caloric restriction is desirable to reduce metabolic activity. The early meals, therefore, should be frequent, small and easily digestible, with salt and caloric content at a minimum level. The Karrel milk diet, 200 cc. of milk 4–5 times a day, fills these requirements. In a few days the patient will desire an increase in diet. Preferably it should still contain approximately 1.0 Gm. of salt a day, but since this requires great care in preparation, a more lenient regimen is acceptable.

TABLE I

CARDIAC GLYCOSIDES
(*Dosage in milligrams*)

Drug	Digitalization (24 hours)		Maintenance Oral
	Intravenous	Oral	
Digitalis Leaf	—	600–1200	100–200
Digitoxin	0.6–1.2	0.6–1.2	0.1–0.2
Digoxin	1.5	—	0.5
Lantoside C	1.0–2.0 (8 hrs.)	—	—
Ouabain	0.7–1.0	—	—
Gitaligen	—	6	0.3

With the use of diuretics, a no-added-salt diet of 2 to 3 Gm. daily is adequate. Salt substitutes may be used to make the diet more palatable. There are many sodium-free substitutes available. Lithium chloride tastes best, but deaths have occurred from its use. Potassium chloride, glutamic acid, and potassium triphosphate in various proportions are used in the commercial salt substitutes. They are a matter of preference and each person must choose his own through trial and error. Perhaps more important is a good cook. Other seasonings, properly used, hide the lack of salt. Herbs, vinegar, lemon, grinder pepper, onions and garlic are some of the other condiments which may be used. In the hospital, where dieticians and adequate facilities are available, such a program of salt restriction is comparatively easy to carry out. However, before the patient is discharged, he must be aware of what is involved in a no-added-salt diet. He will have to have his food prepared separately, use salt-free bread, butter and canned goods, and avoid sodium-containing foods like bacon, processed cheese and commercial ice cream. It is here that the average patient fails and requires special attention.

The mercurial diuretics cause a rapid diuresis, and reduce effectively the excessive extracellular fluid. They diminish the re-absorption of chloride in the renal tubules by depressing the enzyme systems. Of the several good drugs on the market, Thiomerin is most useful. It can be used subcutaneously, whereas most of the others must be given intramuscularly or intravenously. It is advisable to use a test dose of 0.5 cc. to discover any idiosyncrasy. If no difficulty is encountered, the rest of the 1 to 2 cc. dose may be given. This is repeated at intervals of three to four days until "dry weight" is obtained, and the patient is able to lie flat without dyspnea. The response may be followed by watching daily weight or urinary output. If the response is not satisfactory, the action may be reinforced by ammonium chloride (two grams orally three times a day on the interval days). When the patient is failure-free, the period between injections is prolonged; or one of the oral diuretics such as Neohydrin may be used. Frequently, digitalis, rest, and salt restriction will be sufficient if the edema is not severe.

There is danger if the mercurials are used with impaired renal function. In the presence of an N.P.N. over 90, their use carries considerable risk. At times this risk must be tolerated and the drugs given regardless, but great care must be observed. A few erythrocytes or much albumin may be found in the urine as the result of the congestive failure, and will disappear when the failure is relieved.

These drugs are so potent that there is a real danger that electrolytes will be depleted below the desired level. The low salt syndrome is characterized by dehydration, lassitude, apathy, anorexia, increase in the blood urea level, and refraction to further treatment. It is not necessary for the serum electrolytes to be disturbed greatly, because most of the loss is from the interstitial fluid. This syndrome is important because it can be corrected by replacing some of the lost sodium. Hypochloremic alkalosis, which occurs when the chloride ion is reduced, is also important, and easily corrected with ammonium chloride. Other more complicated electrolyte disturbances may occur as terminal events in patients with congestive failure, and their treatment is less satisfactory. Recognition, while difficult, is less important.

Most patients will remain in hospital until maximum control of their failure is evident. Although upon discharge from hospital signs and symptoms may be

relieved, eontinuing therapy is neeessary. Adequate rest with avoidance of fatigue and dyspnea should be emphasized. Digitalis will be required for the rest of the patient's life. Diuretics may still be needed as dyspnea and edema return. Greatest diffieulty will probably be found in the low salt diet, as man eraves salt. With sueh a program, however, one may hope to provide many patients with many useful and happy years.

Summary

Patients in aeute pulmonary edema are treated quiekly and vigorously with morphine, oxygen and venestasis. Patients in ehronic congestive failure are plaeed at rest. Diet control, digitalis and diureties are required.

Acknowledgment

I wish to thank Dr. W. F. Greenwood for his assistance in preparing this article.

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BLOOD TRANSFUSION REACTIONS

D. A. KAVELMAN, 5T6

LOHR provided the first doeumented evidenee of blood transfusion shortly after Harvey's demonstration of the eirculation of the blood in 1628. This experimental work on dogs was soon applied to human subjeets, and within five years so mueh diffieulty was encountered with reaetions that the praetiee of blood transfusion was prohibited by law in both England and Franee. The practice persisted, however, throughout the next 230 years, and was attended in the great majority of eases by blood transfusion reactions. The modern era of blood transfusion may be dated from the reeognition of the existence of blood "groups" and the identification of the basic components of the now familiar

TABLE I

Human Blood Factors Demonstrable by Isoantibodies, Excluding ABO, in the Order of their Statistical Frequency in the Etiology of Blood Transfusion Reactions*

Genetic System	Factors	Alternate Names	Per Cent of Positive Reactions in White Population	
1	D–d	Rh_0–Hr_0	85	63
	C–c	Rh′–Hr′	73	80
	C^w	Rh^w	1	
	E–e	Rh″–Hr″	30	97
2	K–k	Kell–Cellano	8	99.8
3	Fy^a–Fy^b	Duffy	66	82
4	Jk^a–Jk^b	Kidd	77	73
5	S–s		56	88
	M–N		79	71
6	Tj^a	Jay	slightly less than 100	
7	Le^a–Le^b	Lewis	18	72
8	La^a†	Lutheran	8	
9	P†		75	

†Lu^a and P are not important clinically.
*From the work of Levine *et al.* (11).

A-B-O system by Landsteiner in 1900 (2).

The work of Weiner in 1937 led to the complexities of the Rh-Hr system; with the modern methods of detection and identification available at the present time there are over 600,000 known blood types, the commonest of which occurs about once in 200 cases (1). The demonstrable blood factors (excluding the A-B-O family) are summarized in Table I, which is taken from the work of Levine *et al.* (11). It should be noted that 95% of blood transfusion reactions are due to antigens A, B, and D (1), and 97% of reactions other than those caused by A-B-O incompatibility are due to the Rh-Hr system (11).

TABLE II

THE HAZARDS OF BLOOD TRANSFUSION*

1. Those associated with the donor:
   - homologous serum jaundice
   - allergic reactions
   - tropical diseases
     - malaria
     - relapsing fever
     - yaws
     - kala-azar
   - other
     - preclinical measles
     - preclinical influenza
     - post-vaccination reaction
     - post-inoculation reaction
2. Those associated with the stored blood:
   - contamination
     - bacterial
     - viral
   - free hemoglobin
3. Those associated with the act of transfusion:
   - excess of blood
   - air embolism
   - pyrogens
   - thrombophlebitis
   - hemolysis from warming
   - excess citrate
4. Those associated with the recipient:
   - antibodies
   - cardiac or renal insufficiency
   - anemia
   - reagins
   - other

*Modified from J. D. James (9).

REACTION TYPES AND THEIR TREATMENT

The mortality rate from transfusion reactions has been estimated as one per 1000 to 3000 transfusions, even in the best run institutions, with a morbidity rate far in excess of this (6). Blood transfusion, therefore, like marriage, should not be undertaken without full consideration of the risks involved. These risks have been classified by James (9), and his classification is shown in Table II. Of these, we shall consider the hemolytic transfusion reaction at greatest length because of its possible fatal outcome. This reaction depends upon the presence of antibodies in the recipient's serum which will hemolyse the donor's red cells.

A. THE HEMOLYTIC TRANSFUSION REACTION

Two types of hemolytic transfusion reaction have been described by Muirhead (13). The first of these is the *minor incompatible reaction*, characterized by a chill lasting up to 45 minutes followed by a fever of two to six degrees lasting four to eight hours. The fever reaches its peak in one to two hours, with a slow recession to normal over the remainder of the period. This reaction is accompanied by general complaints on the part of the patient, but there is no hemoglobinuria nor any permanent sequellae. The second and more serious type is the *major incompatible reaction.* This also begins with a chill and a fever of two to five degrees, and also is accompanied by general complaints on the part of the patient; however, it is further characterized by hemoglobinemia, hemoglobinuria, and renal failure. The reaction to incompatible blood transfusion depends primarily upon intravascular hemolysis of the donor's cells; this reaction may vary considerably, and in some cases may be entirely absent. The type of reaction produced depends upon

the recipient's antibodies; a high antibody titre is associated with a major transfusion reaction, and a low antibody titre with a minor transfusion reaction.

Any reaction within 24 hours of blood transfusion should be considered to be hemolytic until proved otherwise by clinical and laboratory evidence, as this reaction is the most serious of the hazards of blood transfusion (5). Since intravascular hemolysis is primary in this reaction, a rapid test for the presence of this reaction is provided by centrifuging a specimen of the patient's blood: in cases of hemolytic transfusion reaction the supernatant plasma will be discoloured with free hemoglobin (4).

It has been suggested by Discombe (7) that the kidney may respond as a "shock organ" to some allergic stimuli. He considers the hemolytic transfusion reaction to be an allergic one, and compares the renal lesions found in fatal cases with those found in the crush syndrome. He describes (i) stromal edema with cellular infiltration, (ii) necrosis of the epithelium of the ascending loop of Henle and of the distal convoluted tubule, (iii) the presence of tubulovenous anastomoses, and (iv) the formation of heme-pigment casts in the tubules. This is the basis for the use of cortisone in the treatment of the hemolytic transfusion reaction.

The clinical course of the acute renal failure accompanying a major incompatible reaction is described in three phases (13). The first of these is the phase of *shock*, which lasts a few hours at the most and is characterized by hypotension. The second is that of *renal insufficiency*. It begins within 24 hours with azotemia and oliguria; the blood urea nitrogen rises to a peak of 200–500 mg. per cent in five to nine days, and remains at this level until the patient either dies or recovers. Anuria may last as long as three days, and is superceded by the production of a small amount of urine of low specific gravity. If progress is satisfactory, the 24-hour urine volume will increase with each succeeding day. During this phase acidosis is prominent, and the CO_2 combining power of the plasma may fall to 35 vol. per cent or less. The third and final phase is that of *recovery*, and may be further subdivided into two sub-phases. The first of these is the sub-phase of diuresis, which begins about the fifth to twelfth day; the second is the sub-phase of convalescence, which is a period of one to six months during which the renal function returns to its former state.

Throughout the entire course of the major incompatible reaction it is essential to undertake treatment for shock and to allay apprehension with reassurance and sedatives. Blood loss must be controlled, and replacement therapy undertaken if indicated.

The treatment for renal failure in the hemolytic transfusion reaction is essentially conservative (13). As soon as any sign of a reaction is deteeted, the transfusion is at once stopped. The compatibility of the two bloods is immediately retested by repeating the cross-matching procedure, and a Coombs test is done on the recipient's eells. During phase one, hypertensive drugs such as methamphetamine hydrochloride or 6% dextrose may be given as a slow infusion, as suggested by Discombe (7). It should be noted that patients receiving large amounts of incompatible blood may develop a remarkable hemorrhagic tendency; bleeding may be severe and virtually impossible to control. It is during phase one that any hemorrhagic tendency must be treated; Stage (16) recommends fresh blood, fresh plasma, protamine sulphate, toluidine blue, vitamin K, and splenectomy as various methods of treating this tendency. ACTH and cortisone have been recommended

for use in phase one because of their ability to suppress antibody activity.

The treatment of the phase of renal insufficiency aims at maintaining the patient until such time as the kidneys resume their normal functions. The daily fluid intake is limited to 1000 ml. in excess of the previous 24-hour urine volume, and electrolytes are not used orally or parenterally if they might further distort the chemical pattern of the blood (4). The diet recommended is the Bull-Borst regime (4, 7, 13), which is the administration of the following material by intragastric drip:

Glucose	400 Gm.
Peanut Oil	100 Gm.
Acacia	q.s., to emulsify
Water to	1000 ml.

Penicillin is given routinely in one-quarter to one-half normal dosage (13). In cases where the CO_2C.P. falls below 35 vol. per cent, four to six grams of sodium bicarbonate may be given by mouth in doses of one gram per hour, with a total dose not to exceed ten to thirty grams over a period of four to eight days.

During the diuresis (five litres per day or more) which indicates the beginning of the phase of recovery, replacement of fluid loss six-hourly is essential if dehydration is to be prevented. During this phase the urine chloride should be followed, and sodium chloride replaced as indicated.

B. THE ALLERGIC TRANSFUSION REACTION

The allergic transfusion reaction is by far the most common transfusion reaction, although it is rarely if ever fatal (4). The basis of the allergic reaction is the presence of allergens in the donor's blood which react with reagins present in the recipient's blood to produce urticaria, and less commonly bronchospasm and allergic bronchitis.

Urticaria is treated by a course of one of the antihistaminic drugs. Bronchospasm and allergic bronchitis due to allergic transfusion reaction may be recognized by the concomitant development of an urticarial rash which may be widespread. These reactions are more likely to occur if the same donor is used more than once for the same patient (10). If they are detected during the course of a transfusion, the flow must be stopped at once. Epinephrine (0.5 ml. of a 1:1000 solution) is given subcutaneously and followed by 15 mg. of morphine subcutaneously. If the urticaria persists, it is treated as above with oral antihistamines.

C. THE PYROGENIC TRANSFUSION REACTION

The occurrence of pyrogenic transfusion reactions has been minimized since the advent of the "closed system" for blood transfusion (8). This reaction is due to the presence of pyrogenic protein materials in the infusion bottle and tubing. It usually starts with a shiver, followed by slight headache and fever (10). Should such a reaction occur, the transfusion should be stopped and a new set of tubing used to deliver the remainder of the blood. Positive treatment is minimal, consisting of the administration of 0.6 grams of acetylsalicylic acid or 0.3 grams of Dover's powder in mild cases. The more severe reactions require relief with 15 mg. of morphine or its equivalent.

D. CONTAMINATION OF STORED BLOOD

Blood which has been contaminated in storage causes a febrile response when administered. The contaminant may be either bacterial or viral (14); the most common is a coliform organism which thrives at 4°C. Administration causes a marked chill and fever, along with profound shock (4). This picture is very

similar to that seen in the hemolytic transfusion reaction, but is easily differentiated from it by the inspection of a centrifuged specimen of the patient's blood, as explained previously. Treatment consists of the immediate discontinuance of the transfusion followed by full oral doses of one of the tetracycline group of antibiotics.

E. HOMOLOGOUS SERUM JAUNDICE

This must be distinguished from the jaundice which may accompany the hemolytic transfusion reaction; in the case of homologous serum jaundice the etiological agent is a virus affecting the liver and interfering with the excretion of bilirubin, whereas in the case of the hemolytic transfusion reaction the jaundice is caused by overproduction of bilirubin from the excessive breakdown of red cells.

The transmission of the virus of homologous serum jaundice is one of the most feared of the hazards of blood transfusion (9). The virus may exist undetected in the blood of the donor and be transferred to the recipient, with no apparent ill effect up to 100 days after the transfusion. The mainstay of therapy is prevention by selection of suitable donors; once the disease has become established, only supportive therapy and attempts to relieve the liver of some of its load by low protein diets are available.

PROPHYLAXIS

In blood transfusion, as in many other fields, the old adage "an ounce of prevention is worth a pound of cure" stands firm in spite of the onslaught of modern methods of therapy. To prevent transfusion reactions, primary consideration must be given in each case to the *necessity* for transfusion (15, 17, 19). The following items have been suggested by Davidsohn as a guide to the indications for transfusion (6):

1. acute hemorrhage
2. oligemic shock
3. gastrointestinal hemorrhage
4. hemorrhagic disease
5. platelet transfusion in thrombocytopenic purpura

These indications are sufficiently narrow to exclude the so-called "cosmetic" transfusions, which are far more useful in the treatment of the patient's relatives than in the treatment of the patient himself. It should be noted that platelet transfusion must be given with silicone-coated tubing and needles.

Once it is ascertained that transfusion is indicated in a given case, steps must be taken to select a suitable donor. This must be done for the protection of *both* donor and recipient. Trumbull (18) states that the following are causes for the rejection of a donor:

1. a history of malaria
2. a positive serological test for syphilis
3. a history of jaundice or viral hepatitis
4. a history of active tuberculosis
5. a history of heart disease
6. pregnancy or miscarriage within the preceding six months
7. the presence of skin lesions
8. a history of allergy
9. a history of bleeding abnormalities

The blood of the donors not eliminated by this selection procedure is then cross-matched with the recipient's blood. In the past it has been the practice to perform this test using saline suspensions of the red cells involved; this procedure, however, fails to detect Rh-Hr incompatibilities. Brown (3) recommends the general adoption of cross-matching in native serum or bovine albumin, with complete avoidance of saline; this de-

tects the majority of incompatible antibodies and does not require any further equipment than that in use at present. It prevents the administration of Rh-incompatible blood, and thus the sensitization of the patient to such blood by transfusion (16). This is particularly important in the case of young women. "Universal donor" blood should be avoided except in dire emergency (19).

Many of the transfusion reactions caused by incompatibility are caused by inexperience or carelessness (14, 19). The surest safeguard against such unnecessary reactions is to have the pre-transfusion grouping and cross-matching done by properly trained personnel who are constantly available. Wiener (19) suggests that medical students who have been properly trained may be used in the technician's off-hours to perform these tests. An additional source of error is that bottles of blood may be labelled incorrectly, or may be administered to the wrong patient; the only means of prevention possible here is strict vigilance by all personnel at all times.

The use of the plasma volume expanders is coming to the fore in the prophylaxis of blood transfusion reactions, but they themselves are not without attendant dangers. The most satisfactory available are Dextran and Plasmosan, but their greatest use at present is to allow time for proper pre-transfusion testing before the administration of whole blood. They thus provide a service in eliminating undue haste, the greatest enemy of a safe, smooth blood transfusion.

Summary

A classification of the hazards of blood transfusion has been presented, and five of these hazards have been discussed. The greatest emphasis has been placed on the hemolytic transfusion reaction, with consideration of its etiology, clinical course, and treatment. The allergic transfusion reaction, the pyrogenic transfusion reaction, contamination of stored blood, and homologous serum jaundice have been discussed at lesser length.

A consideration of the generally accepted safeguards of blood transfusion has been included in the section on prophylaxis. Pre-transfusion procedures are accorded a major place in this discussion, for it is only through proper use of these procedures that any significant reduction in the number of blood transfusion reactions can be achieved. Plasma volume expanders are mentioned briefly.

The work which began with Landsteiner at the turn of the century must be carried to its ultimate conclusion: the complete elimination of blood transfusion reactions from our hospitals. It is to be hoped that the combination of training, vigilance, and research will achieve this aim and make a blood transfusion reaction as rare as a case of smallpox or diphtheria.

Acknowledgements

It is a pleasure to acknowledge my indebtedness to Dr. R. E. Haist, Dr. E. A. Sellers, and Dr. J. F. Paterson, for reading and criticizing my original manuscript. Dr. John Hunter, of the Defence Research Medical Laboratories, was particularly helpful with his encouragement as well as his criticism during its preparation.

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A REPORT ON YOUR MEDICAL SOCIETY

W. S. HUNTER, 5T6

The Medical Society. *Your* Medical Society. What is it? What does it do? What have I to do with it? These questions are those which many of the undergraduate students of the Medical Faculty never quite speak out loud, but which seem to pervade the lecture room atmosphere whenever some of the Society's activities are mentioned. What each student should realize is that *he* is the Medical Society and the Society is the medical and premedical student body as a whole . . . . . the society of medical students. What each student should realize is what Dr. Gordon Cameron, a past president of the Society, stated a few years ago, "The strength of any democratic body lies less in the planning of its elected councils than in the interest and participation of its members."

You are the Society. The group of people you elect to office in the spring make up "the Assembly" of the Society. The Society was formed "to serve the welfare and interests of the medical undergraduate body"; the Assembly is the governing body, charged with the general business and finance of the Society. This group, the Assembly, meets every second Wednesday to conduct the Society's business.

You, your Society, under the guidance of the Assembly, carries on the following activities:

The Medical Journal.
The Medical Athletic Association.
The Medical Women's Undergraduate Association.
Daffydil.
The Medical Arts and Letters Club comprised of 4 groups:
- The Medical Music Club.
- The Osler Society.
- The Medical Debating Society.
- The Medical Glee Club.

The Medical At Home.
The Medical Common Rooms:
1. T.G.H. Common Room.
2. The Duncan Room.

The Medical Float in the Home-Coming Week Parade.
The Medical Staff-Student Smoker.
The Staff-Student Curriculum Committee.
The Meds-Pot dance.
Freshmen Initiations.

The Assembly also provides support for the Toronto CAMSI Committee and liaison with the SAC.

These activities are organized for the benefit of the Society members, for you. Further, any group of students with some

interest in common may form their own club or association, and will be helped in their purpose by the Assembly.

What have you personally to do with this? Let the above quotation stand, "The strength of any democratic body lies less in the planning of its elected councils than in the interest and participation of its members". (Firstly) all of the above-listed activities need your support if they are to carry on as they were so enthusiastically begun many years ago. (Secondly) look around you and realize that from your group or your class has come or will come the people to continue these activities—to maintain the excellent standards set by students who have gone before us.

May we urge you then to participate in these activities of your society: to play volleyball, to help to write your class Daffydil skit, to debate, to go to your class parties, to help to build decorations for the At Home, to help to produce the Journal. If you have thought that you would like to take part in some activity, then do not delay—go ahead, take part, you *will* enjoy yourself. May we add that from supporters come the leaders, the future Journal editors, future Daffydil directors, future club presidents, future Society executive.

Equally, if not more important, may we urge you to accept a nomination for a position on your year executive, on the Assembly, or in a club or association to which you belong. You probably will do a good job, you probably will enjoy it, you probably will gain some useful experience, but you never *will* know unless you try.

Lastly, may we urge you to be well informed of your Society's business, to give voice to your complaints or suggestions, through your elected representatives.

The Medical Society, *your* Medical Society, an association with a strong record and revered past, can only be stronger through your active interest.

Respectfully submitted,

W. S. Hunter, *President.*

ABSTRACTS

The Management of Systemic Arterial Hypertension: Kirkendale, W. M. and Culbertson, S. W. Arch. Int. Med. **95:** 601, 1955.

The authors discuss their experience with the management of patients suffering from (i) "essential" or primary hypertension and (ii) secondary hypertension where eradication of the primary cause is either impractical or does not give relief.

Emphasis is placed on the need for accurate diagnosis and assessment (Grading I–IV) of the patient for correct management and evaluation of results. No specific series of patients is discussed.

General measures such as rest, reassurance and weight reduction were found to be very valuable in milder cases (Grades I–II) and in many cases obviated the need for specific hypotensive preparations.

Sodium restriction in the order of 2–300 mg./day is advocated and said to reduce substantially the blood pressure in one-half to one-third of cases.

Hypotensive drugs are discussed regarding pharmacological action, indications, dosage, results and side-effects:

(i) Rauwolfia derivatives particularly benefit milder cases with a psychoneurotic element and may be used alone or with other preparations.

(ii) Hydralizine used alone shows many side-effects and poor long term control and is therefore best used in conjunction with other drugs, chiefly of the methonium groups.

(iii) Veratrum preparations have only intermittent effectiveness, and cause nausea, but are good in hypertensive crises such as hypertensive encephalopathy, eclampsia, and pre-eclampsia, where they may be given IV.

(iv) Ganglionic blocking agents were found impractical in mild cases owing to the need for close supervision, and are therefore reserved for severe cases (Grades III–IV) and may be used with Hydralizine and Rauwolfia preparations.

(v) Other drugs such as adrenergic blockers and Hydergine are found to be of little value.

(vi) Surgical treatment (sympathectomy) is conceded to be of value in severe cases and young hypertensives.

The special treatment of hypertension in hypertensive encephalopathy, cerebrovascular accidents, congestive failure and uremia is also discussed.

G. A. deVeber.

An Evaluation of the Effect of Continuous Long-term Anticoagulant Therapy on the Prognosis of Myocardial Infarction: A Report of 82 Cases. Suzman, M. M., Ruskin, H. D., Goldberg, B. Circulation, **12**: 3, 1955.

Based on the hypothesis that a sustained hypoprothombinemia maintained by continuous anticoagulant therapy would retard further thrombus formation in myocardial infaretion, the authors considered it rational to apply this therapy on a long term basis with a view to preventing recurrences of coronary thrombosis. 82 patients chose to accept this regimen for periods varying from 3 to 76 months following the presenting attack of myocardial infarction. Parallel observation of a control series of 88 patients treated with anticoagulants only in the acute phase of the disease allowed a comparison between the effects of long and short term therapy. The anticoagulant most commonly used was Dicumarol, in weekly doses averaging 350–450 mg., aiming at a prothombin time of twice the normal. Adequate control necessitated tests at intervals of one to two weeks or longer, depending on the stability of the prothombin levels.

Statistical analysis of the observations yielded the following results:

1. The total mortality in the long term group (7.3%) was significantly lower than that in the control group (33%). Further importance is attached to this by the increased incidence of both previous coronary artery disease and a severer presenting attack in the group which chose long term therapy.

2. The recurrence rate of myocardial infarction in the long term group (8.3%) was significantly lower than that in the control (27.3%).

3. Of the severe cases with a history of previous infarction, the mortality rate in the long term group (14.3%) was significantly lower than that in the control group (66.6%).

4. There were 12 cases of hemorrhage among the 82 on long term therapy. One death was attributed indirectly to anticoagulant over-effect.

The authors conclude from their study that long term anticoagulant therapy is of definite value in improving the prognosis after myocardial infarction, especially in those cases with a severe presenting attack and a history of previous infarction.

J. L. Naiman.

The Selection of Patients with Mitral Stenosis for Valvular Surgery: Ellis, L. B., Am. Pract., 8: No. 4, Aug. 1955.

A. Patients with mitral stenosis are grouped as follows:

Group I. Patients without significant symptoms. These are not operated upon.

Group II. Patients with symptoms which are not progressive or handicapping. These should not be operated upon unless the patient will not or cannot accept his disability, in which case operation is recommended.

Group III. Patients with progressive pulmonary symptoms but without evidence of congestive heart failure. At any time they may slip into group IV or die of pulmonary edema. Operation is *urgently* indicated.

Group IV. Patients who have or have had congestive failure. Many feel that these are inoperable; others accept them, often with good results.

B. Factors affecting operative risk include:

Mitral insufficiency. This contraindicates operation. However, in spite of accurate clinical investigations, a great number of patients may come unsuspectingly to operation. When doubt exists cardiac exploration is indicated as the operative risk is low.

Auricullar fibrillation. This adds the risk of dislodging an embolus.

Calcification. Risk of dislodging a calcific fragment exists. Also, the results may be poor because of the difficulty of mobilizing a calcified valve.

Associated disease of the aortic valve. If aortic stenosis or insufficiency are of significant degree operation is contraindicated. In certain doubtful cases the author recommends that mitral valvuloplasty be done and that the surgeon also operate on the aortic valve if necessary. If aortic stenosis is low grade, as indicated by simultaneous pressure tracings from the left ventricle and the aorta, then only mitral valvuloplasty is indicated and the hazardous double procedure is avoided.

Age. Age per se is no contraindication.

Associated disease. Associated disease of any sort demands consideration and if of marked degree constitutes a relative contraindication. Patients with pulmonary disease, fibrosis, or emphysema are a greater risk to the anaesthetist in that they are peculiarly susceptible to hypoxia.

C. Results:

On the basis of 750 patients operated upon by Harken at the Boston City Hospital, the following results were obtained. Eighty-one per cent of those surviving operation in groups II and III showed moderate to marked improvement and most were restored to virtually normal health. The results in group IV are less striking but are impressive when one considers the desperate states in which the patients presented. Sixty-three per cent were substantially improved. The operative mortality in groups II and III was less than 2%; in group IV it was 20%.

D. Comment:

The operation is not a cure, and even though it may be lifesaving it is only palliative. It does not restore the valves to normal nor does it prevent recurrences of rheumatic fever or the danger of future bacterial endocarditis.

L. Charendoff.

Types of Death in Acute Myocardial Infarction: McQuay, N. W., Edwards, J. E. and Burchell, H. B. Arch. Int. Med. **96:** 1, 1955.

A study was made of 133 patients dying in hospital of acute myocardial infarction in which necropsy was performed. The types of death were classi-

fied as follows: coronary failure (31), rupture of the heart (20), myocardial failure predominately left ventricular (17), myocardial failure predominately right ventricular (29), combined right and left (11), shock (12), thromboembolic phenomena—systemic (4), pulmonary (4). Only 53 of 133 patients did not show evidence of some form of healed myocardial infarction. The incidence of acute transmural infarction was greater in this group, whilst acute subendocardial infarction with myocardial failure was more common in those who showed healed infarction.

The commonest single cause of death was designated "coronary failure". This is characterized by a syndrome of recurring pain after infarction, but without recurring infarction. In many cases myocardial failure preceded infarction. The common underlying causes of failure were hypertension or previous infarction or both. Rupture of the heart was much commoner in women. The study gives no support to the assumption that anticoagulant therapy renders the patient more vulnerable to rupture. Rupture occurred only in patients with transmural infarction, and was of the ventricular septum in 6 cases and of the free wall in 14. 6% of patients died of embolism, half pulmonary and half systemic.

In considering these results it must be borne in mind that the group of patients studied all died in the acute post-infarctive period, and represent only a small proportion of all cases of myocardial infarction.

J. R. Wilkes.

The Anterior Chest Wall Syndrome—Chest Pain Resembling Pain of Cardiac Origin: Prinzmetal, M. and Massumi, R. A. J.A.M.A. **159:** 177, 1955.

The authors call attention to a painful somatic affection of the anterior chest wall in patients with and without a history of myocardial infarction. The syndrome occurs very commonly from weeks to months after coronary occlusion; otherwise, the history is negative. The condition occurs less commonly in patients without a history of coronary occlusion.

Symptoms include steady pain spreading throughout the anterior chest wall, most severe in the sternal region and precordium, with no radiation. If left untreated, the pain may last for months or years. The pain is subject to sudden, acute, spontaneous exacerbations, often excrutiating, brought on by certain positions or movements of the body or chest. It has no relation to physical exertion or meals. The duration is a matter of hours and it terminates gradually. The intensity is steady during hours of activity but subsides during the night. Emotional stress seems to have an aggravating effect. Glyceryl trinitrate is without effect, but relief may be obtained with narcotics. The pain is not associated with increased perspiration, salivation, or systemic symptoms, but mental depression, anxiety neurosis and addiction to narcotics are commonly encountered.

Physical Examination reveals finger-tip tenderness of the anterior chest wall, the pressure producing non-radiating local pain most pronounced over cartilage and bone. The area of maximum tenderness corresponds to the points of greatest pain. The skin is normal and there is no evidence of nerve involvement. Blood cell count, E.S.R., urinalysis, and x-ray are normal. E.C.G. taken during the acute attacks and between attacks is unchanged, although hyperventilation (frequently seen in such patients) may lead to minor E.C.G. changes.

The author differentiates this condition from other diseases leading to persistent pain in the anterior chest wall.

The histopathology and the possible

mechanism of the pain are also discussed.

Treatment. Prompt improvement with a therapeutic diagnostic test with corticotropin, cortisone and radiation therapy may provide a clue to the correct diagnosis. Institution of proper physical therapy, breathing exercises and muscular exercise may be all that is necessary to correct this condition.

D. Glick.

OF CURRENT INTEREST

Alpha Omega Alpha, Honour Medical Society, is pleased to announce the election of the following new members: Dr. W. Hurst Brown, Dr. R. I. Macdonald, Dr. Trevor Owen, J. Q. Bliss, J. D. Carson, F. A. Green, W. H. Kerr, Miss F. E. McQueen, J. L. Naiman, W. F. Neale, S. J. Revich, M. Spivak, S. M. Sumi, A. S. Trimble, P. M. Watson, J. M. Harvey, R. I. Hector, L. H. Mudie. The initiation banquet was held on November 14th, at the King Edward Hotel, where the guest speaker was Dr. W. E. Blatz, Professor of Psychology.

* * *

The following new appointments and promotions to the Faculty Council were made from July 1, 1955:

Dr. M. H. Brown has been promoted to head of the Department of Hygiene and Preventive Medicine. Other promotions are: to the rank of Associate Professor: R. J. Wilson (Hygiene & Preventive Medicine); D. N. Henderson and H. W. Johnston (Obstetrics & Gynaecology); F. C. Monkhouse and A. M. Rappaport (Physiology); J. W. L. Doust (Psychiatry); W. G. Bigelow (Surgery); to the rank of Assistant Professor: C. R. Burton, C. C. Gray, W. F. Greenwood, W. E. Hall, D. B. Moran, M. A. Ogryzlo and W. A. Oille (Medicine); J. Mann and G. L. Watt (Obstetrics & Gynaecology); W. G. Carscadden, J. T. T. Russell, W. M. Spooner, C. H. Watson, A. W. M. White (Surgery).

Dr. J. K. W. Ferguson, head of the Department of Pharmacology, became director of the Connaught Medical Research Laboratories upon the retirement of Dr. R. D. Defries on October 1, 1955.

* * *

Professor R. M. Janes has been appointed President of the Canadian Association of Clinical Surgeons.

* * *

Dr. W. G. Bigelow of the Department of Surgery was awarded the medal of the International Society of Surgery, in Copenhagen in July, for outstanding work in the field of hypothermia. Dr. Bigelow is the first recipient of this award.

* * *

Dr. R. I. Harris is on a five month trip around the world as the Sir Arthur Sims Commonwealth Professor of Surgery of the Royal College of Surgeons of England. Dr. Harris will give lectures and clinics in hospitals and universities in New Zealand, Australia, Singapore, Delhi and Great Britain.

* * *

Dr. Terence Molony has been awarded the O'Keefe Fellowship in Otolaryngology.

* * *

The Donald C. Balfour Lecture in Surgery was delivered by Sir Harry Platt, F.R.C.S., President, Royal College of Surgeons of England, on October 26th,

1955, in the Best Institute. The subject of the lecture was "The Back-Ache Sciatica Problem".

* * *

The following awards have been made:
The John McRae Memorial Scholarship
W. F. Neale, 5T6
No. 4 Canadian General Hospital
Scholarship ..... J. D. Mull, 5T7
No. 4 Canadian General Hospital
Scholarship ..... J. H. Chizen, 5T7

* * *

Professor C. H. Best received the honorary D.Sc. degree from the University of Maine on August 12, and delivered the Convocation address.

Professor R. M. James has been elected President of the Royal College of Physicians and Surgeons of Canada.

Dr. Harry Bakwin, President, American Academy of Paediatrics, delivered a lecture at the Hospital for Sick Children, on October 26th. The subject—"Delinqueney in Children—Etiologieal Factors".

Dr. J. P. Gray gave a lecture on Medical Writing, on October 27th, in the Medical Building. This lecture was sponsored by the American Medical Writers Association and Parke Davis Company.

Dr. Edward J. Stieglitz of Washington, D.C. delivered a lecture in the Banting Institute on October 28th. The subject—"Rclativity in Health".

Dr. R. D. Defries, former director of Connaught Medical Research Laboratories, has been awarded a Lasker Foundation Award for his work on the Canadian Salk vaccine programme. He will be presented with it at the meeting of the American Public Health Association in Kansas City on November 17th.

The following awards have been made:
R.C.A.M.C. Women's Auxiliary Bursary
Miss B. E. Pearson (IV Med. Yr.)
Phi Delta Epsilon Med. Fraternity
Bursary .... M. Spivak (IV Med. Yr.)
G. Roy Sproat & Katherine Sproat
Bursaries —
Miss S. J. Wallace (III Med. Yr.)
Miss M. G. Norman (II Med. Yr.)
Scottish Rite Masons Bursary
A. C. Strickler (II Med. Yr.)
Samuel Godfrey Scholarship
B. R. Oliver (I Premed. Yr.)
Medical Alumni Scholarship
L. M. Jerry (I Premed. Yr.)
Harvey Harnick Seholarship
H. I. Adelman (I Premed. Yr.)
George Armstrong Peters Prize in
Surgery ..... W. J. Lougheed, M.D.

RECENT ACCESSIONS TO THE MEDICAL READING ROOM

Ackerman, L. V.: **Surgical pathology.** 1953.
Alexander, H. L.: **Reactions with drug therapy.** 1955.
Asboe-Hansen, G.: **Connective tissue in health and disease.** 1954.
Burch, G. E.: **Primer of cardiology.** 2 ed. 1953.
Boies, L. R.: **Fundamentals of otolaryngology.** 2 ed. 1954.
Copeman, W. S. G.: **Cortisone and ACTH in clinical practice.** 1953.
Hosler, R. M.: **A manual of cardiac resuscitation.** 1954.
Lowden, T. G.: **The casualty department.** 1955.
Methods in biochemical analysis. David Glick ed. v. 1, 1955.
Murphy, A. L.: **The story of medicine.** 1954.
New York Academy of Medicine. **The musculosketal system.** 1952.
Perkins, G.: **The foundations of surgery.** 1954.
Shaw, J. H.: **Fluoridation as a public health measure.** 1954.
Sperry, W. L.: **The ethical basis of medical practice.** 1950.
Sulzberger, M. B.: **The clinical significance of disturbances in the delivery of sweat.** 1955.
Welch, H.: **Principles and practice of antibiotic therapy.** 1954.
World Conference on Medical Education, 1st, London. 1953.
Bett, W. R.: **History and conquest of common diseases.** 1954.
Boyden, E. A.: **Segmental anatomy of the lungs.** 1955.
Brockington, C. F.: **The principles of nutrition for practitioner and student.** 1952.
Chargaff, E.: **The nucleic acids.** v. 1–2, 1954/55.
Christopher, F.: **Minor surgery.** 7th ed. 1955.
Courville, C. B.: **Contributions to the study of cerebral anoxia.** 1953.
Cornell conferences on therapy. v. 1–7, 1954.
DePalma, A. F.: **Diseases of the knee.** 1954.
Dubos, R. J.: **Biochemical determinants of microbial diseases.** 1954.
Edwards, H. E.: **Recent advances in surgery.** 4th ed. 1954.
Fleming, A. J.: **Modern occupational medicine.** 1954.
Greep, R. O.: Histology. 1954.
MacIntosh, R. R.: **Local analgesia in abdominal surgery.** 1953.
Mendlowitz, M. **The digital circulation.** 1954.
Moseley, H. F.: **An atlas of musculosketal exposures.** 1955.
Sebrell, W. H.: **The vitamins; chemistry, physiology, pathology.** v. 1–3, 1955.
Shaw, W.: **Textbook of operative gynaecology.** 1954.
Shryoch, R. H.: **The unique influence of the Johns Hopkins University on American Medicine.** 1953.
Stein, I.: **Living bone in health and diseases.** 1955.
Stevenson, L. G.: **Nobel prize winners in medicine and physiology.** 1953.
Wolff, E.: Diseases of the eye. 4th ed. 1953.

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Husband often the carrier. "Approximately 39 to 47 per cent of resistant cases are reinfections from the sexual partner."[1] Whittington reports infestation in the male in 27 per cent[2] and Freed in 28.5 per cent.[3] A study of all foci of infection, such as urethra, prostate, seminal vesicles, bladder, kidneys, pelvis and preputial sac, would probably reveal even higher incidence in the male.

Danger without signals. Trichomonads in the male rarely produce symptoms to signal their presence.

Prevent re-infection. Karnaky recommends in recurrent cases that the husband wear a condom during coitus for four to nine months. By the end of this time the trichomonads will usually die out. Davis states: Use of a sheath by the husband has long been advised during the period a woman is under treatment and should be used permanently if he carries the infection.

Prescribe quality condoms. To eliminate trichomonads "once and for all," take specific measures to win co-operation of

the husband. In prescribing a condom, be selective as to quality and take advantage of Schmid product improvements.

Prescribe protection. Take specific measures to win the co-operation of the husband in your treatment of vaginal trichomoniasis. Otherwise he may re-infect the patient and nullify the good results of the regimen. Any husband or wife in your practice would most likely prefer to hand the druggist your prescription for a condom, rather than to ask for it "in public." This is another instance of diplomacy in medicine to prevent an embarrassing situation. To assure finest quality and earn appreciation for your thoughtfulness, prescribe condoms by name. Prescribe Schmid protection for as long as *four to nine months* after the wife's infestation has cleared. The protection Schmid condoms afford is the very foundation of re-infection control.

References: 1. Karnaky, K. J.: Urol. & Cutan. Rev. 48:812 (Nov.) 1938. 2. Whittington, M. J.: J. Obst. & Gynaec. Brit. Emp. 58:614 (Aug.) 1951. 3. Freed, L. F.: South African M. J. (March 27) 1948, as abstracted in Urol. & Cutan. Rev. 52:489 (Aug.) 1948.

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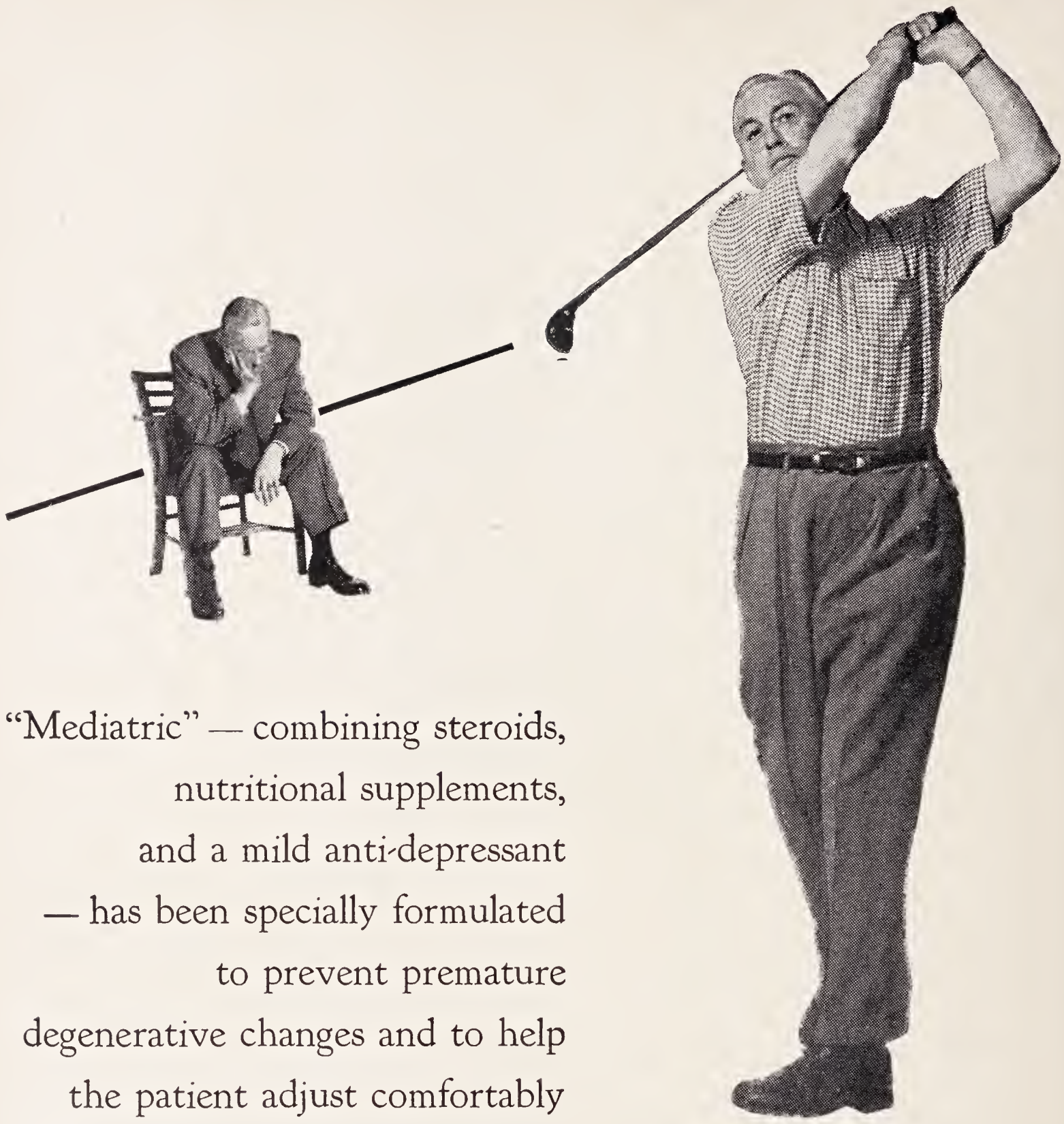

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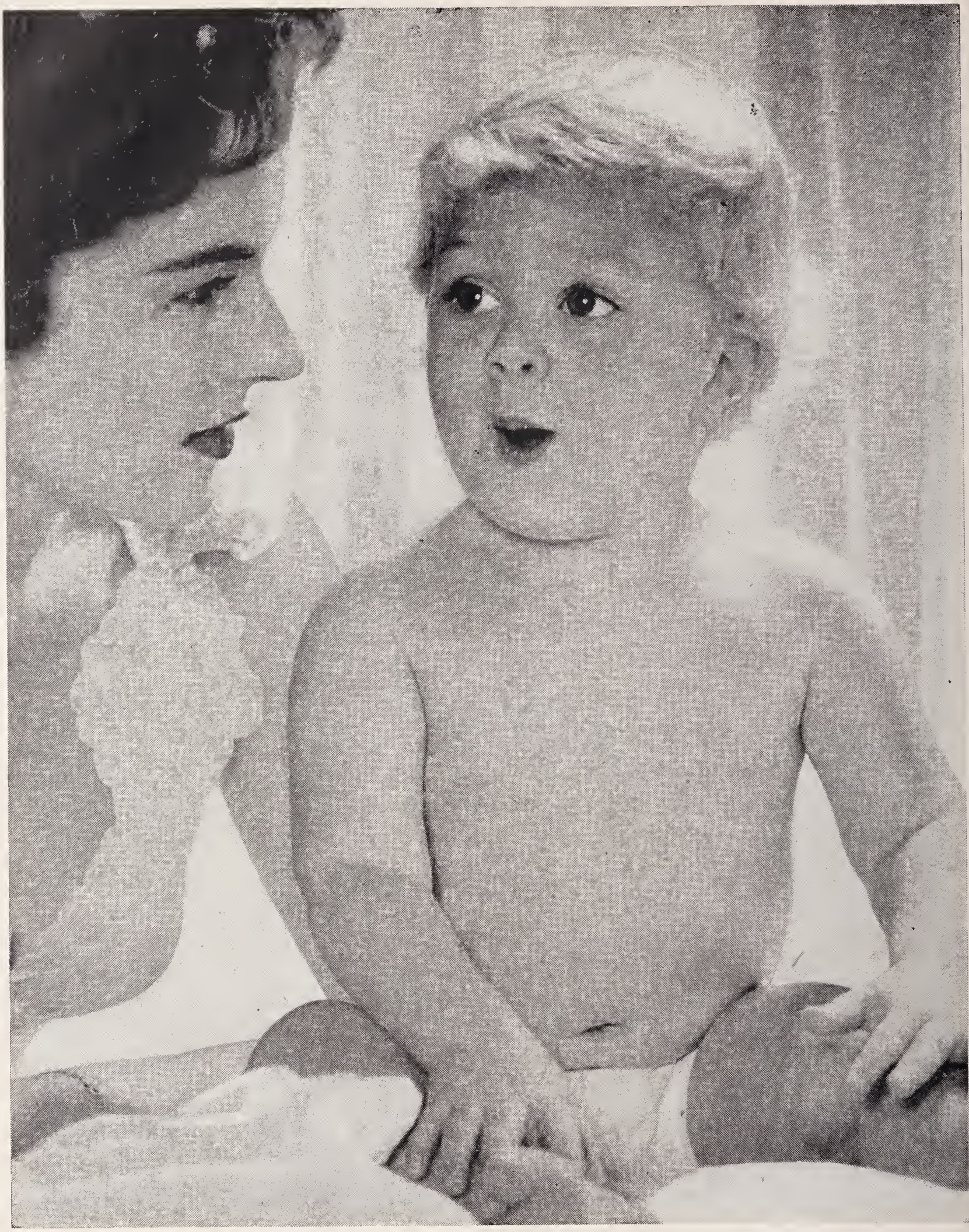

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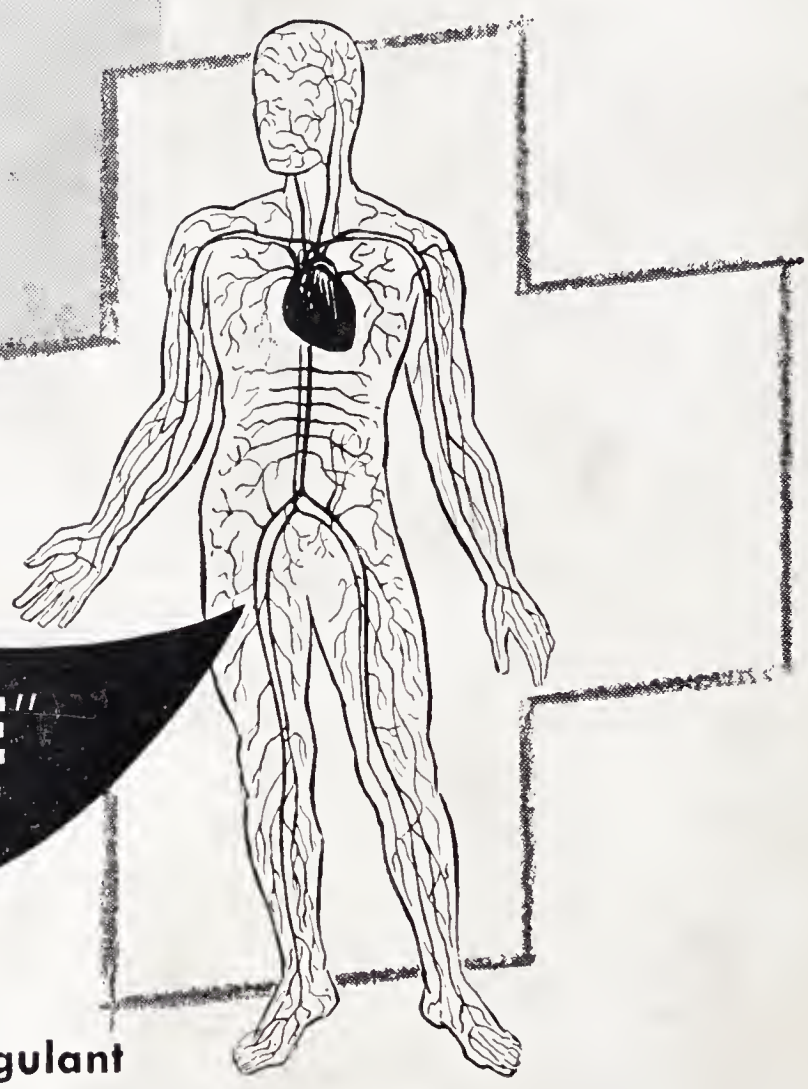

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